The Egyptian Journal of Hospital Medicine (April 2018) Vol. 71 (7), Page 3667-3675

Evaluation of Central Auditory Processing in Egyptian Multiple Sclerosis Patients

Gehan A. El-Zarea[1] Amany A. Shalaby[2], Hussin M. Hussin[3], Mohammad S. Ali[1]

1- Audiology Unit, Department of Otolaryngology, Faculty of Medicine – Al-Azhar University,
2- Audiology Unit, Department of Otolaryngology, Faculty of Medicine – Ain-Shams University,
3- Department of Neurology, Faculty of Medicine – Al-Azhar University, Cairo, Egypt

ABSTRACT

Background: Many multiple sclerosis (MS) patients with normal peripheral hearing suffer from difficulties in their hearing especially speech perception in background noise, which is possibly because of deficit of central auditory processing in this group.

Objective: To elaborate the effect of MS on central auditory processing.

Subjects and methods: Seven audiologic tests including masking level difference (MLD), auditory memory test (recognition, content and sequence), dichotic digit test (DDT), speech intelligibility in noise test (SPIN) and gap in noise test (GIN) as well as electrophysiologic assessment (speech evoked ABR c-ABR and P300) were used for comparing aspects of central auditory processing between MS patients and controls. Scores for each test obtained through cross-sectional non-invasive study conducted on 30 Egyptian subjects with relapsing-remitting MS who had mean age of 37.07 ± 11.43 years, and 30 controls with normal peripheral hearing and mean age of 33.40 ± 9.38.

Results: This study demonstrated reduced MLD in MS at 500 & 1000 Hz in relation to controls. MS patients were worse than controls in recognition memory (pv = 0.011), memory for contents (pv <***0.001***) and memory for sequence (pv **<*0.001***). in addition, low scores of DDT (version I & II) revealed in MS patients (pv = **<*0.001***& 0.011 for I & II respectively), reduced SPIN test score in MS subjects (pv**<*0.001***), elevated threshold and reduction of percent of correct answer obtained from GIN test in MS patients (*Pv* **<*0.001***). Furthermore, in MS patients, there were prolonged latencies and reduced amplitudes of c-ABR waves and P300. In addition, significant differences were revealed between MS subjects and controls in all c-ABR measures analysis.

Conclusion: this study revealed apparent effect of MS on auditory processing.

Keywords: Multiple Sclerosis, Central Auditory Processing, Egyptian Multiple Sclerosis patients.

INTRODUCTION

Multiple sclerosis (MS) is a Central Nervous System (CNS) disorder characterized by inflammation, demyelination and neurodegeneration, which results in impairments in multiple domains. Also, central auditory nervous system (CANS) can be included**.** Because of the widespread development of the myelin destructions, MS results in a broad range of symptoms, which include motor, cognitive, and neuropsychiatric problems**.** In Egypt, A community-based survey in Al Quseir, Egypt, has found an MS prevalence of 13.74/100,000 [1]**.**

The CAP constitutes a series of mental operations that the individual performs when dealing with information received via the sense of hearing and can be described simply as “what the brain does with what the ear hears”. Efficient CAP involves a series of auditory skills that are vital in the listening and communication process, these include auditory discrimination, sound localization, auditory attention, auditory figure-ground, auditory closure, synthesis, auditory analysis, auditory association and auditory memory [2]**.**

Valadbeigi *et al.* [3] concluded that the people with MS suffer from some degree of disorder in the temporal resolution which might be due to involvement of CNS and, somehow, deficit in CAP. Therefore, for evaluating the temporal resolution in people with multiple sclerosis, GIN test could be useful.

Aim of the work: To elaborate the impaction of MS on central auditory processing.

SUBJECTS AND METHOD

Subjects: This study was conducted on two groups; **Patients group,** 30 Egyptian patients with definite MS (relapsing remitting type) according to revised McDonald criteria 2010 (9 males, 21 females) aged from21 to 53 years with a mean age of 37.07 ± 11.43 were selected from the Neurology out-patient clinic of Al-Hussin University Hospital during the period from March 2016 to September 2017. **Control group,** 30 healthy subjects, Egyptians were selected from volunteers (16 males and 14 females) with a mean age of 33.40 ± 9.38. They were demonstrated no auditory complaints in everyday listening situations. Normal peripheral hearing sensitivity was required in both groups. Written consents were taken from all subjects.

Received:20 / 3 /2018 DOI: **10.12816/0047690**
Accepted30: / 3 /2018

Research Ethic Committee of Al-Hussin University Hospital approved the study.

METHODS

Equipment: Sound treated room, clinical 2-channel audiometer (Interacoustic version AC40) accompanied by the SONY Compact Disc Player, a interacoustics loud speakers located in the sound booth, and Telephonics TDH-39P supraaural headphones. Immittancemetr: GSI middle ear analyzer (Autotymp. version 39) and Smart EPs Intelligent hearing system (IHS) software Version Microsoft Windows XP Intel 2007 Bios.

All participants were subjected to the following: Full history taking, administration of the Arabic auditory skill questionnaire, otological examination **basic audiological evaluation** in the form of: Pure Tone Audiometry (PTA); air conduction at frequencies between 250-8000 at octave interval. Bone conduction threshold at frequencies between 500-4000, also at octave interval. Speech audiometry (SRTs and Word Discrimination Score. And Immittancemetery (tympanometry and acostic reflex).

Central auditory tests: Diagnostic batteries to assess the integrity of CANS include behavioral and electrophysiologic procedures. In this study we focused on behavioral tests used to identify lesions (including diffuse lesions), abnormalities, or dysfunction of the CANS, as well as identify associated functional deficits (e.g., listening in noise deficits).

Behavioral assessment:

MLD test: to evaluate the ability of the CANS, to receive information in both ears and to unify them in a perceptual event; it is believed that this unification occurs in the brainstem**.**

Stimuli: The signal was a 500 Hz and a 1000 Hz pure tones pulsed mode, and temporally centered in the masker. Maskers were narrow band noise (NBN). Both signal and noise were presented binaurally at 60 dB HL to compare the listener's signal threshold for a variety of masking conditions where both signal and noise are presented binaurally; ***homophasic condition:*** signal and noise in phase**,** ***antiphasic condition:*** signal out of phase & noise out of phase.

Procedure: The MLD was measured by presenting a pulsed pure tone signal binaurally with simultaneous presentation of NBN. The first condition should be to find the threshold for the homophasic condition (S0N0). Then, the antiphasic conditions (SπNo & SoNμ). The task of the listener was to respond "yes" that tones were heard in the noise or "no" that tones were not heard in the noise.

Auditory Memory tests: All the developed speech materials were recorded in sound studio, by the voice of an experienced male opera singer with typical Egyptian dialect.

1.Recognition Memory Test: Five lists of Arabic bisyllabic words available for this test. Each list consisted of 11 words which will be repeated twice, to form a list of 22 bisyllabic words. The subject was instructed to raise his hand each time he heard a repeated word in the same list. **Scoring:** For each list, by subtracting wrong responses from eleven. Final scoring is by calculating the mean of the five lists.

2.Memory for Content Test: Two groups of lists (A) and (B) available for memory for content test. Each group consist of eight lists of monosyllabic simple Arabic words. The first list comprised of two words. The number of words increased gradually to reach nine words in the eighth list. The subject was instructed to repeat the whole list he had just heard irrespective of its sequence. ***Scoring:*** The highest number of words the candidate can memorize is taken as his score

3.Memory for Sequence Test: Two other groups of words (A) and (B) available for this test and different from those used in memory for content test. Each group consist of seven lists. The first list consist of two words and the number of words gradually increased throughout the seven lists, to reach eight words in the last list. The Subject was asked to repeat the words in the same order. **Scoring:** Highest number of words can be memorized in the same order is taken as the score.

(3) Dichotic Digits test*:* Two versions of the test, carried out simultaneously in both ears at 70 dBHL. Version I: The subject was heard one digit in one ear and simultaneously heard a different digit in the other ear. Version II; The subject was heard two digits in one ear and simultaneously heard two different digits in the other ear. The task in two versions was to repeat back all two or four digits presented to both ears. The 3 to 10 waveform arabic digital files. Measures obtained following testing involved a percentage correct out of possible 100%.

Speech Intelligibility in Noise test*:* Eight lists of pre-recorded Arabic Phonetically Balanced words (25 words in each list) with background speech noise (multi-talker babble). two randomly selected lists are presented (one to each ear) in multi-talker babble at zero SNR at 70 dBHL from a CD player. The subjects were instructed to ignore the noise and concentrate on the words only to repeat the words presented. The number of correctly identified words were calculated as a percent correct score of each ear.

GIN test: The test is composed of a series of 6-sec segments of broadband white noise that contains 0 to 3 silent intervals (gaps in noise) of durations of 2, 3, 4,5, 6, 8, 10, 12, 15 and 20 msec. The individual gap durations are presented 6 times each in random locations across the various trials, for a total of 60 gaps.

Procedure: The test stimuli were presented monaurally at 70 dB HL. The subjects were instructed to press the response button as soon as they heard a gap. ***Score:*** The correct detection score and the gap detection threshold, which is defined as the shortest gap duration that the patient can identify**.**

Electrophysiologic measures

(1) c-ABR

Electrode montage: Three Ag/ AgCl electrodes were fixed according to the Smart-EP manual specification: One high frontal Fz (positive electrode)**,** one low frontal Fpz (ground electrode) and the last one was placed on right mastoids (reference electrode). The electrode impendence was kept below 5 KOhms.

Stimulus parameters: A consonant vowel syllable 40-ms /da/ syllable that consist of onset noise burst during the first 10 ms and formant transition between the consonant and a steady-state vowel figure (4) at 80 dBSPL with rate of 7.4/sec alternating polarity

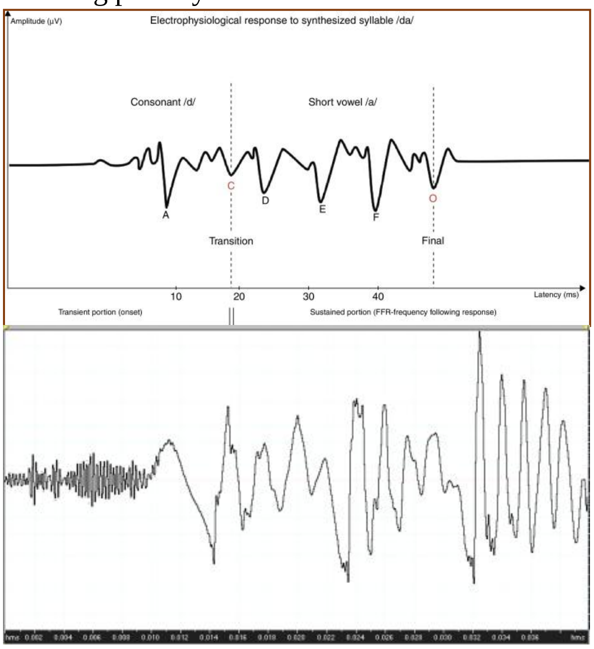

Figure (1): Rt: Waveform of/da/ 40 msec stimulus **Lt:** Representation of electrophysiological response to synthesized syllable /da/. Personal file of the investigator of an assessment performed with BioMARK™ software [4]**.**

- **Recording parameters:** Two subaverages of 3000 sweeps were collected. Band pass filter setting of 100 to 3000 Hz. Analysis period of 60 msec. An artifact criterion of ± 31 µV was applied to reject epochs that contained myogenic artifacts. Gain was set to 100,000. Right ear only was stimulated in this study. So, the advantage of right ear in encoding speech by contralateral projection to the left hemisphere**.**
- **Response analysis:** For each subject, an average was obtained by averaging all responses (6000 sweeps) to the original (Alternating) stimulus (an average for the 2 trial traces). Then, manually saved as a text file using AEP to ASC II convertor program and then they were entered the brainstem toolbox for spectral and temporal analysis by using of MATLAB (version 2014, MathWorkInc, Natick, MA, USA).

c-ABR is characterized by transient peaks as well as sustained elements that comprise the frequency following response (FFR). The response to the onset of the speech stimulus /da/ includes a positive peak (wave V), likely analogous to the wave V elicited by click stimuli, followed immediately by a negative trough (wave A). Following the onset response, a series of peaks (C to F) represent FFR. Offset response is represented by wave O (Figure 5).

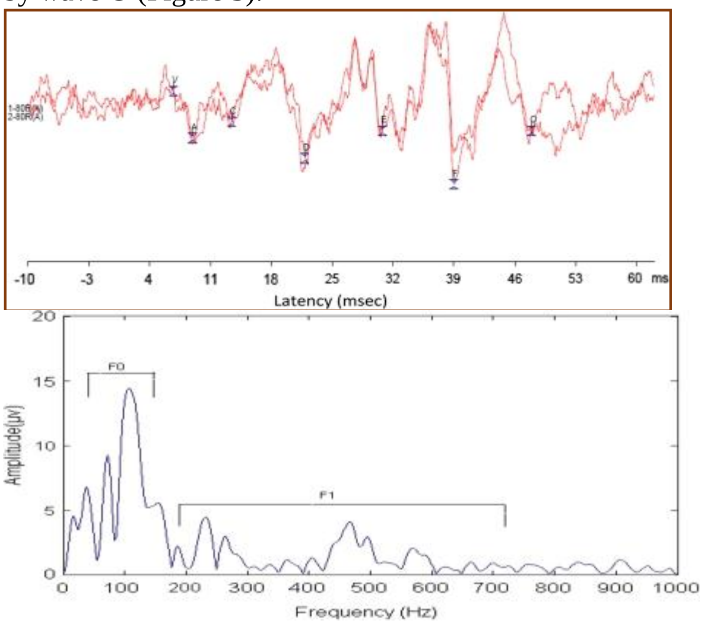

Figure (2): Rt: Speech Evoked ABR recorded in one of the subjects. Lt: Analysis of F0 and F1. Response indicates that only the fundamental frequency and first formant frequency (F0 = 103–121 Hz; F1 = 220–720 Hz) were measurable [4]**.**

Peak Latency and Amplitude**:** Peak latency and baseline to peak amplitude of all waves were measured.

Transient measure analysis: Onset response (latencies, amplitude of peak V & A) and V/A complex measures (latency, amplitude, slpoe and area). Offset response (latency and amplitude of peak O).

Sustained measure analysis (FFR): FFR region include the area between Wave C and O (11.4 to 40.6 ms). The following analysis techniques were employed to analyze the FFR:

Root Mean Square (RMS) amplitude: The magnitude of neural activation over a given time.

Cross-correlation: To compare the timing and morphology of the two signals. In the current study we perform Stimulus-to-response (S-Rr) correlations**.**

Fast Fourier Transform (FFT): FFT analysis was conducted on the temporal response waveforms obtained for each subject to determine the distribution and magnitude of energy in the FFR spectrum. As the FFR represents neural phase locking to the envelope (F0) and TFS (F1) of the stimulus, we expected to see maximal energy at peaks in the FFR spectrum corresponding to the fundamental frequency (F0: 103 – 121 Hz) of the stimulus, representing the envelope (E) and the first formant (F1: 454 – 719) frequency of the stimulus, representing the temporal fine structure encoding (TFS).

(2) P-300 (auditory event related potential): P-300 component identified as positive peak that follow the negative N200 in specified latency window (e.g. 250-700 ms) in the infrequent response waveform [12]**.**

An auditory "oddball" paradigm was used to elicit P300 responses. 250 monaural (at right ear) acoustic stimuli at frequencies of 1000 Hz for the frequent (80%) and 2000 Hz for the rare (20%) at 80 dB SPL in time window of 510 milliseconds with rate of 1.1/sec to the right ear only**.**

-Electrode montage: Right Inverting (-): right ear mastoid (A_2). Non-Inverting (+): vertex (Cz), use a Y-adapter to join channels. Ground: low forehead (F_{pz}), in accordance with the international 10–20 system***.***

-Procedure: The subjects were lying comfortably awake in a semi-darkened sound-treated room. Skin was cleansed with gauze and abrasive paste. Surface electrodes were then placed over electrolytic paste (for optimizing electrical conductivity) and fixed with microporous adhesive tape. The electrode impendence was kept below 5 KOhms, with a difference of up to two ohms between electrodes. Individuals remained seated and were instructed to pay attention and count out loud the number of occurrences of the rare stimulus, and to avoid artifact contamination caused by eye movement, subjects were asked to keep their eyes fixed on a target.

Response analysis and measurement: P300 wave was selected as the wave with the highest positive peak after the N1-P2-N2 complex. then marked the latency and amplitude of P300 on this curve. To obtain amplitude values of the P300 wave, the cursor was placed on the positive polarity wave (P300) as far as the negative polarity (N2)

Waveform identification: Identification of the location of the P300 as the positive peak which occurs between 300-400 msec. P300 latency and P300 amplitude also, obtained.

RESULTS

Data were collected, coded, revised and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The data were presented as number and percentages for the qualitative data, mean, standard deviations and ranges for the quantitative data with parametric distribution and median with inter quartile range (IQR) for the quantitative data with nonparametric distribution. ***Chi-square test*** was used in the comparison between two groups with qualitative data and ***Fisher exact test*** was used instead of the Chi-square test when the expected count in any cell found less than 5. ***Independent t-test*** was used in the comparison between two groups with quantitative data and parametric distribution and ***Mann-Whitney test*** was used in the comparison between two groups with quantitative data and non-parametric distribution. ***Spearman correlation coefficients*** were used to assess the significant relation between two quantitative parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

$P > 0.05$: Non- significant (NS). $P < 0.05$: Significant (S). $P < 0.01$: Highly significant (HS)

As mentioned above, the results of this study as regard basic audiological evaluation showed that all studied subjects within normal peripheral hearing. In addition, there were no significant differences between MS subjects and controls neither in PTA threshold, SRT, WD%, nor immittancemetry. Also, there were difference between right ear and left ear in all studied subjects. Results categorized based on the outcomes of central test battery results as follows:

Behavioral central tests: With different degrees, this study revealed significant difference between MS patients and controls in all conducted tests including MLD at 500 & 1000 Hz, auditory memory tests (recognition, content and sequence), DDT (Version I & version II), SPIN score and

GIN (gap detection threshold and correct answer ratio) table (1).

By means of correlations between psychophysical and electrophysiologic measures, there were significant positive correlations between P300 amplitude and memory for content.

Table (1): Comparison between MS & Control groups as regard psychophysical tests.

		MS				Control				Independent t-test	
		Mean	SD	95% Confidence Interval for Mean		Mean	SD	95% Confidence Interval for Mean			
				Lower Bound	Upper Bound			Lower Bound	Upper Bound	T	P-value
MLD test	MLD 500	5.97	1.16	5.55	6.38	9.13	1.28	8.67	9.58	2.403	0.009
	MLD 1000	6.10	1.16	5.68	6.51	9.80	1.06	9.42	10.17	2.244	0.008
Auditory memory test	Recog Mem (%)	80.98	10.45	77.24	84.71	91.71	5.14	89.87	93.54	2.347	0.011
	Content (Words)	4.57	1.07	4.18	4.95	6.37	0.61	6.15	6.58	3.409	<0.001
	Sequence (Words)	4.10	0.92	3.77	4.42	5.93	0.64	5.70	6.15	9.219	<0.001
DDT	DDT1 (%)	83.08	4.22	81.56	84.59	88.25	2.57	87.33	89.16	3.476	<0.001
	DDT2%	75.37	3.08	74.26	76.47	80.70	2.76	79.71	81.68	2.348	0.011
SPIN	SPIN (%)	77.93	5.58	75.93	79.92	91.60	2.72	90.62	92.57	6.961	<0.001
GIN test	GIN thr (ms)	8.10	1.39	7.60	8.59	5.13	0.91	4.80	5.45	2.746	0.004
	GIN ratio (%)	70.14	8.14	67.22	73.05	85.37	5.19	83.51	87.22	6.521	<0.001

This table shows that there was statistically significant difference in all psychoacoustic tests MS and control groups.

Electrophysiologic measures:

c-ABR results

this study revealed significant differences between MS subjects and controls in all parameters of c-ABR including transient and sustained measures analysis. In addition, prolonged latencies and reduced amplitudes of c-ABR in MS subjects in relation to controls were found (figure 3).

P300

The finding in this study showed that their prolonged latency and reduced amplitude of P300 wave in MS subjects versus controls. Also, a positive correlation between memory for content and P300 amplitude was revealed. This because that P300 mainly express memory component in auditory event related cortical potential (figure 4).

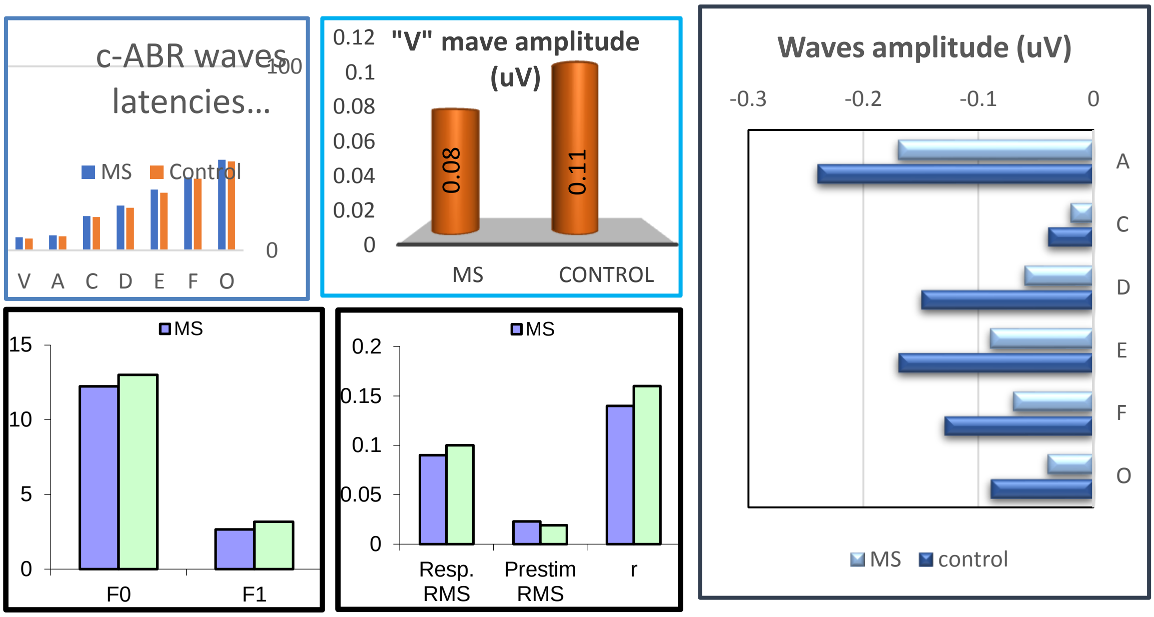

Figure (3): comparison between MS patients and controls as regard c-ABR parameters. The three histograms belong to wave's latencies and amplitudes. the lower Rt one belongs to fundamental and first formant frequencies magnitude. the lower left one belongs to root mean square of response (Resp RMS), prestimulus RMS and stimulus-response correlation.

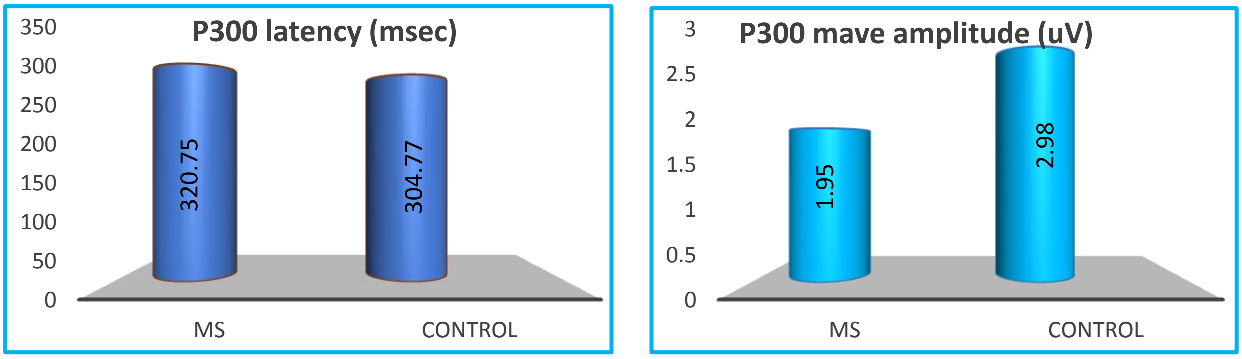

Figure (4): comparison between MS subjects and controls as regard P300 latency and amplitude.

DISCUSSION

Because the auditory system consists of a series of connections that allow processing of sounds from the external ear up to the auditory cortex of the brain, a disruption to these signals anywhere along the auditory pathway can result in diminished reception of auditory information**.** In addition, cognitive impairment is frequently occurring in 40–70% of MS patients even during the early stages of the disease; that could be impact central auditory performance regardless its form [5]

In this study, CAP was assessed using both behavioral and electrophysiologic test battery for MS and control subjects, with consideration of anatomical and physiological central auditory pathway.

Behavioral tests

MLD test: The finding in this study revealed significant reduced MLD at 500 Hz and 1000 Hz in MS subjects in relation to control subjects. These findings compatible with ***(Musiek et al.)*** [6] hese findings probably related to fact that the demyelination in MS induced an impairment of binaural processing due to the demyelination of many pons structures, such as the superior olives and a region between the two inferior colliculi, that are responsible for this function**.**

Auditory memory test[7]**:** within all domains tested of auditory memory, the MS patients performed worse than the controls. Minor, but also significant impairments were found for recognition memory. The most significant difference between MS patients and controls was in sequence memory. Also, highly significant difference between patients and controls in memory for content domain. With respect to type of memory test, similar findings have been obtained from several previous studies. for example:

Pelosi et al. [8] investigated working memory and short-term memory, by auditory event-related-potentials in early MS patients by recording both auditory and visual ERPs during the memorizing as well as the recognition and matching of digits of a short-term memory paradigm. They found that working memory impaired in early MS patients as compared with healthy controls. Although, these abnormalities have been referred to about both modalities, abnormal changes were more noticeable in the auditory modality. Moreover**,** ***Muthuselvi and Yathiraj*** [9] reported that, auditory memory was noted to be one of the most predominately affected auditory processes. ***Wilson et al.*** [10] found a weak but significant (p= < 0.05) correlations of auditory memory subtests and the diagnostic CAPD tests.

Dichotic Digit Test*:* In this study, there was significant difference between MS patients and controls in DDT scores. These results suggest that, MS patients have deficit in dichotic listening, since both components of DDT evaluate dichotic listening, which requires transmission of information between the cerebral hemispheres via the corpus callosum. Because the corpus callosum is a highly myelinated structure, it seemed reasonable that patients with MS might have dichotic listening deficits because of impaired transmission of auditory information across the corpus callosum. Several investigations reported that subjects with MS are likely to have problems with dichotic listening ***(Jacobson et al.)***[11]

In contrast with these studies, we did not find significant differences between right and left ears as regard DDT agreed with ***Lewis et al.***[12] but disagree with other studies. This could be explained by that these studies have been conducted on different types of MS rather than relapsing remitting type. We hypothesized that this difference may be a result of the high linguistic and short-term memory demands associated with both dichotic tests used rather than DDT (i.e., words) versus the DDT (a closed set of numerical digits).

SPIN test: In this study, MS Patients performed worse than controls in word discrimination in noise despite excellent speech discrimination in quiet environment, which is similar to the study of ***Lewis et al. & Valadbeigi et al.,*** Speech is one of the most complex forms of pattern recognition and requires both spatial and temporal processing. As speech understanding problems in background noise are features of individuals with auditory processing problems and disorders of the CANS, one might postulate that individuals with MS would also have this type of deficit. In fact, several studies revealed that a high percentage (33–69 %) of individuals with MS had trouble in speech understanding when they exposed to a competing stimulus.

GIN test: GIN test was used to assess temporal resolution**.** Results showed significant difference between normal subjects and MS patients in both parameters. No significant difference between the right and left ears was observed between the two groups. The GIN had two independent test measures; the approximate threshold and the total percent of correctly repeated gaps. According to Musiek [16], the approximate threshold yields better sensitivity and specificity than the total percent of correctly repeated gaps. According to results of the GIN test, it became obvious that in patient with MS, temporal resolution performance was poorer than the healthy group. These findings agreed with ***Lewis et al. & Valadbeigi et al..***

In 2005, GIN test was used in 50 normal people and 18 patients with significant lesions in CANS. Results indicated that the average approximate threshold in the right ear was 8.5 ms and 7.8 ms for the left ear that showed weaker performance of temporal resolution in people with CAPD. Given the overlap of the two results it can be mentioned that CAP in people with MS is impaired [16.]

Electrophysiological tests:

1- Speech evoked ABR

c-ABR applied as an effective biomarker of CAPD that may be present in various diseases. In addition, for evaluation of CAP in adults with normal hearing, elderly, hearing aid and cochlear implant users and evaluation of auditory rehabilitation program**.**

In the present study, all studied subjects had reliable and replicable c-ABR response. With 100% detectability for all c-ABR waves except C wave (detected in 66.66% of MS subjects and 93.33% of controls) and O wave (detected in 83.33% of MS subjects and 100% of controls). This indicates significant difference between MS and controls only in detectability of C and O waves. These results agreed with ***Vender-Werff and Burns*** [13] who found that C and O waves were the least detectible.

These findings were already expected, because although the generating sites had not yet been defined, the literature showed that the sustained portion of the c-ABR already assesses the auditory pathway up to the subcortical level**.** Therefore, it suggested that this absence of waves is related to an auditory processing disorder, even which could not have captured by the behavioral tests. Subsequently, other authors showed that even with the onset of the waves, an alteration in the auditory processing can be detected by the delay of the latencies

An interesting fact found in previous studies is that the results of the click-evoked ABR corroborated those found for the c-ABR, as both evaluations suggest an alteration in the auditory processing, even though they not comparable**.**

Sanfins et al. **[14]** described presence of a statistically significant difference in the latency of D wave of c-ABR, with higher values for the study group of children with CAPD. Nevertheless, all studies reinforced the idea that the c-ABR may be useful tool to assess CANS accurately.

As regard the correlation between psychophysical and c-ABR measures, there were no correlation between c-ABR measures and behavioral tests except for the MLD at 1000 Hz that showed positive correlation with F0 (p value 0.049). This agree with ***Sanguebuche et al.*** **[15].** The main explanation was that the generating site for the selective attention skill is in the lower brainstem**.** Thus, It became clear, that the c-ABR does not depend on these structures. Therefore, these subjects have a physiological alteration in CANS, as detected by the waves of the c-ABR, even they have normal responses in the behavioral tests. Thus, they showed a division of neural function in the brainstem. This shows the impartiality of the physiological and behavioral responses for processing tests that involve the lower brainstem, in which temporal resolution and selective attention begin.

On the other hand, MS had clear impact on c-ABR response consequently on brainstem encoding of speech stimulus /da/. In general, there were prolonged latencies and reduced amplitudes of all c-ABR waves. Also, all transient and sustained c-ABR measures were affected with variable degrees.

Auditory event-related cortical response (P300)

In this study, P300 results show abnormal delayed latency and reduced amplitude in MS patients relative to controls, demonstrating that the disease had affected the higher levels (cortical areas) of the auditory pathway. These finding in agree with the studies of ***Polich et al.* [16] *; Joy and Johnson* [17]).** However, some researchers found that no abnormalities in the LAEPs of patients with MS. Like, ***Schochat et al.*[18] and *Folmer et al.* [19]** this might be most patients in these studies had not progressed to the point where neural transmission was impaired enough to affect AERP component latencies. Because the P300 is considered a "cognitive" ERP component, reduced P300 amplitudes in MS might reflect impaired cognition or compromised transmission of information from the auditory system to higher-order processing regions of the brain. So, P300 is considered as useful tool used to assess central auditory functions as well as cognitive processing abilities in MS patients**.**

Conclusion: Standard audiologic tests have focused on disorders of peripheral system and do not show the precise dysfunction of the central system. Some fundamental audiologic tests including MLD, Auditory memory test, DDT, SPIN and GIN test used in this study, along with other behavioral and electrophysiological ones can be used for monitoring the effectiveness of medication, rehabilitation and related therapies. Auditory memory deficits in MS patients may be due to cognitive impairment or because of CAP affection by MS pathology. C-ABR is a useful tool in speech encoding process along auditory pathway even with normal behavioral test results.

Recommendations: This study completed with a relatively small number of subjects. MS is a heterogeneous disease that is quite variable between patients and within patients over time. Therefore, large-scale study with different types of MS individuals would add to the understanding of the effect of different types of MS on auditory process.

REFERENCES

1- **Tallawy H, Farghaly W, Rageh T *et al.* (2013):** Door-to-door survey of major neurological disorders (project) in Al Quseir City, Red Sea Governorate, Egypt. Neuropsychiatr Dis Treat., (9): 767-971.

2- **Mendonça E, Muniz L, Leal M *et al.* (2013):** Applicability of the P300 frequency pattern test to assess auditory processing. Brazilian Journal of Otorhinolaryngology; 79 (4): 512 – 521.

3- **Valadbeigi A, Weisi F, Rohbakhsh N *et al.* (2014):** Central auditory processing and word discrimination in patients with multiple sclerosis. Eur Arch Otorhinolaryngol., 271(11): 2891–2896.

4- **Sinha S and Basavara V (2010):** Speech Evoked Auditory Brainstem Responses: A New Tool to Study Brainstem Encoding of Speech Sounds. Indian J Otolaryngol Head Neck Surg., 62(4): 395–399.

5- **Magnano I, Aiello I and Piras M (2006**): Cognitive impairment and neurophysiological correlates in MS. J Neurol Sci., 245(1-2):117–122.

6- **Musiek F, Shinn J, Jirsa R *et al. (*2005):** GIN (Gaps-In-Noise) test performance in subjects with confirmed central auditory nervous system involvement. Ear and Hearing, 26 (6): 608-618.

7- **Tawfik S, Abdel Maksoud A and Abumoussa H (2002):** Assessment of attention and memory in scholastic underchievers: psychological and electrophysiological studies. Unpublished MD thesis. Ain Shams University, Cairo, Egypt.

8- **Pelosi L, Geesken J, Holly M *et al.* (1997):** Working memory impairment in early multiple sclerosis. Evidence from an event-related potential study of patients with clinically isolated myelopathy. A. journal of neurology, 120 (11): 2039–2058.

9- **Muthuselvi T and Yathiraj A (2009):** Utility of the screening checklist for auditory processing (SCAP) in detecting (C)APD in children. Student Research, (7):159-175.

10- **Wilson W, Jackson A, Pender A *et al.* (2011):** The CHAPS, SIFTER and TAPS-R as predictors of (C)AP skills and (C)APD. Journal of Speech, Language, and Hearing Research; 278 (54): 278–291.

11- **Jacobson J, Deppe U and Murray T (1983):** Dichotic paradigms in multiple sclerosis. Ear Hear., (4): 311–317.

12- **Lewis M, Mcmillan G, Hutter M *et al.* (2012):** Preliminary Identification of Central Auditory Processing Screening Tests for Individuals with Multiple Sclerosis. Semin Hear., (33): 261–273.

13- **Vander Werff K and Burns K (2011):** Brain stem responses to speech in younger and older adults. Ear and Hearing,32 (2): 168- 180.

14- **Sanfins M, Borges L, Ubiali T *et al.* (2017):** Speech-evoked auditory brainstem response in the differential diagnosis of scholastic difficulties. Braz J Otorhinolaryngol., (83):112–116.

15- **Sanguebuche T, Peixe B, Bruno R *et al.* (2017):** Speech-evoked Brainstem Auditory Responses and Auditory Processing Skills: A Correlation in Adults with Hearing Loss. Int Arch Otorhinolaryngol., 22 (1): 38-44.

16- **Polich J, Romine J, Sipe J *et al.* (1992):** P300 in multiple sclerosis: a preliminary report.International Journal of Psychophysiology, 12 (2):155–163.

17- **Joy J and Johnson R (1997):** Multiple sclerosis current status and strategies for the future. Neurology, (48): 270-272.

18- **Schochat E, Matas C, Sanches S, Carvallo R and Matas S (2006**): Central Auditory Evaluation in Multiple Sclerosis. Arq. Neuropsiquiatr., 64 (3-B): 872-876.

19- **Folmer F, Hutter M, Lilly D *et al.* (2012):** Electrophysiological Measures of Auditory Processing in Patients with Multiple Sclerosis. Seminars in Hearing, (33): 274-282.