DISCUSSION

Auditory neuropathy spectrum disorder is a pathology so named because it appears to involve dysfunction of VIIIth nerve fibers and/or the inner hair cell-VIIIth nerve synapse. [14, 62] In individuals with ANSD, OAEs and CM are typically present. However, the auditory brain stem response (ABR) is either absent or grossly abnormal, beginning with wave I, which reflects VIIIth nerve activity. The abnormal ABR is felt to reflect poor synchrony in the auditory nerve. This pathology provides a naturally occurring condition, where OHCs of the cochlea are normal but both afferent activity and efferent regulation of the cochlea are impaired. [14]

The contribution of the efferent system in the pathogenesis of ANSD should not be neglected. As it is known that presenting of contralateral noise leads to suppression of the transient evoked OAEs (TEOAEs) and distortion product OAEs (DPOAEs) by 1-3 dB. [169, 170] This contralateral suppression phenomenon was attributed to the stimulation of the efferent system through the medial olivo-cochlear bundle (OCB). Consistent with the pathology of ANSD, those patients characteristically show an abnormal olivo-cochlear reflex measured by absence of contralateral suppression of OAEs. [7, 171]

It is known that contralateral presentation of noise may interfere with the perception of sound, through the peripheral mechanism mediated via the olivocochlear efferent neurons, middle ear muscle system and through the central masking mechanism. [1, 2]

Central masking is thought to occur during auditory processing, when sound information travels beyond the ears and is processed within our vast neural networks. [2] Zwisklocki et al (1972) suggested that, central masking posits a mechanism of overlapping excitation or interaction between contralateral signals at some points in the central auditory nervous system. It is used to explain the threshold shift and amplitude reduction occurred in the tested ear resulting from the introduction of masking signal in the non-tested ear. [4] This is unlike peripheral masking that describes the ipsilateral masking phenomenon, which occurs in the cochlea or cochlear nerve where monaural threshold elevations can be attributed to the physical overlap of masker and probe signal in the auditory periphery.

Some authors suggested that the amount of central masking effect to be about 5 -7 dB, [160] however; threshold shift as large as 15-18 dB have been reported. [4, 162] Also, the effect increases with the increment of the amplitude of the masking noise.

It is assumed that central masking is a phenomenon that is mediated by the efferent system, especially by the medial olivocochlear bundle (MOCB). Physiological findings revealed that the MOCB provides a mechanism for central feedback and for control of activity at the auditory periphery. It is suggested that this control is provided by the anatomical and functional relationships of the outer hair cells (OHCs) with the efferent system. This notion is supported by animal studies in which central masking was reduced or eliminated when the MOCB was sectioned at the floor of the IVth ventricle in macaque monkeys. [2]

Smith et al [2] (2000) and other authors investigated the role of MOCB in central masking. [172, 173] Smith et al (2000) found that the contralateral masking effect was eliminated when the MOC fibers were sectioned at the floor of the fourth ventricle in

macaque monkeys. [2] The results of those studies indicate that contralateral masking produces changes in cochlear mechanics that are known to be mediated by the MOC fibers. [2,152, 172, 173] It means that, intact efferent pathway is needed in order to show masking effect.

The current study was conducted on ten adult participants (20 ears) diagnosed with ANSD. They ranged in age from 15 to 53 years and attended the Audiology Unit, the E.N.T. Department, Alexandria University Hospital. The subjects ranged according to the degree of hearing loss, from mild to moderate degree. Ten ears had mild degree of SNHL and ten ears had moderate SNHL. Two frequencies (500 and 4000 Hz) were evaluated. Thresholds of hearing at the two frequencies for 40-Hz and 80-Hz ASSR potentials were measured before and after introducing contra lateral broad band noise of 70 dB HL in intensity.

Single channel monotic ASSR was carried out using the GSI AUDERA evoked potential system with test signals that were modulated at rates of 74 and 95 Hz at 500 and 4000 Hz, respectively. 100% Amplitude modulation and 10% frequency modulation were combined to maximize response amplitude.

I. Gender and age effect:

In this study, there was no evidence of an effect of gender on ASSR responses. Regarding the wide age range of our studied adults, research has generally shown that ASSR responses do not change with age in adults. Picton et al (2002) described the results of a group of 30 subjects from 20 to 81 years of age in which no significant changes in the amplitude or phase of ASSR across different ages were found. [174]

II. Degree of hearing loss:

In the current study, the subjects were selected as having a hearing loss up to moderate degree. This degree was selected to ensure the presence of measurable ASSR response.

III. Pure tone audiometry in ANSD patients:

Low-frequency/rising audiometric contours were observed in about 70% of this sample of adults suffering from ANSD as shown in table (2) and figure (6). In previous studies, the audiometric patterns of patients with ANSD of low-frequency/rising audiograms were observed about two thirds of ears. [175] The high-frequency hearing loss configuration most commonly seen with sensorineural type hearing loss was only observed in approximately 10% of cases in those studies.

Most reports on ANSD published before the mid-1990s described subjects with audiograms in the mild to moderate hearing loss range. [176- 178] This bias towards losses of lesser degree may reflect that many of these early patients were only identified as a result of the inconsistency between behavioral and electrophysiologic findings. Starr *et al.* (2000) found average hearing levels in 31% of ears at less than 35 dBHL, 39% of ears between 35 and 70 dBHL, and 30% of ears at more than 70dBHL. [22] Madden *et al.* (2002) also found an even spread of behavioral audiograms, with 6 (33%) in their group of 18 affected

children presenting with audiograms in the normal-to-mild range, 6 in the moderate-to-severe range, and 6 in the profound hearing loss range. [179]

IV. Analysis per patient:

In the current study, comparison between amount of suppression (difference between before and after noise) that measured in right ear and left ear was done. The subjects that had unilateral response or no response at any frequency in either potential were excluded from analysis. No significant correlation was found between the two ears as shown in table (3). That result indicated that, although the neural pathways of suppression of both ears are somewhat interfered in the brainstem, but this interference had no effect on amount of suppression.

V. Analysis per degree of hearing loss:

Another comparison was done between mild and moderate degrees of hearing loss to assess the effect of the degree of hearing loss on the process of suppression. No significant difference was found between the two degrees indicating that amount of hearing loss - up to moderate degree- does not affect suppression as shown in table (4).

VI. Effect of contralateral noise:

In the present study, 40-Hz and 80-Hz ASSR thresholds at CFs of 500 and 4000 Hz were measured before and after presentation of contralateral noise signal. Then, before and after masking thresholds were compared. Comparison was done by using the mean and standard deviation (SD) in tables (5-8) and figures (13,14). The effect of contralateral suppression was assessed in 20 ears. The ears that had no ASSR response at any tested frequency were excluded from the analysis.

There was statistically significant suppression by the contralateral BBN for the 40-Hz ASSR at 500 and 4000 Hz demonstrated by the result of Paired t- test, where the value of P was 0.003 and less than 0.001 at the two CFs, respectively, as shown in tables (5,6) and figure (13).

For the 80-Hz ASSR, there was statistically significant suppression by the contra lateral BBN at 500 and 4000 Hz demonstrated by the result of Paired t- test, where the value of P was 0.016 and 0.001 at the two CFs, respectively, as shown in tables (7,8) and figure (14).

Despite of the presence of statistically significant suppression of the two ASSR potentials, the clinically significant suppression needs a higher value of threshold elevation to be considered.

Suppression magnitude was assessed in the current study as (10 to 15 dB) threshold elevation, to detect the clinically significant suppression that occurred with contra lateral noise presentation. This value was set according to the results of a study was done by Maki et al (2009) investigating the effects of contra lateral noise on both 40- and 80-Hz ASSRs in normal subjects, that contra lateral noise caused significant threshold elevation (average 10 to 15 dB). [12]

In the current study, the 40-Hz potential at 500 Hz recording showed one ear out of eighteen ears (that already had ASSR response) that had clinically significant suppression of 10 dB and six ears had 5 dB threshold elevation. At 4000 Hz, three ears out of eighteen ears showed clinically significant suppression of 10 dB in two ears and 15 dB in one ear and eight ears had 5 dB threshold elevation.

For 80-Hz potential measurement at 500Hz, four ears out of eleven ears (that already had ASSR response) had 5 dB threshold elevation with no clinically significant suppression. At 4000 Hz, one ear out of eighteen ears had 10 dB threshold elevation and nine ears had 5 dB threshold elevation.

In summary, in 40-Hz ASSR, one ear at 500 Hz and three ears at 4000 Hz had clinically significant suppression. In 80-Hz one ear at 4000 Hz showed the clinical suppression. So, we can conclude that contralateral noise did not cause clinically significant suppression of ASSR potentials at 500 and 4000 Hz frequencies.

In 1992, Galambos and Makeig studied the effect of contra lateral noise on ABR and 40-Hz ASSR in normal subjects, using clicks [164] and tone pips [180] as stimuli in two separate experiments. They found that contra lateral noise has large suppressive effects on the click and tone-burst evoked 40-Hz ASSR, reducing the amplitude about one-half of the control value, but no significant effects on ABR waves. They interpreted those results to mean that contra lateral masking effect occurs at the cortical level of auditory pathway, central to the location of wave V generator in the brainstem.

Considering the different contralateral sound effects between the ABR and 40-Hz ASSR, different effects could also be expected between the 40- and 80-Hz ASSRs. Maki et al (2009) investigated the effects of contra lateral noise on both 40- and 80-Hz ASSRs in 11 normal hearing subjects. [12] ASSRs were measured using the multiple ASSR (MASTER) technique. Test stimuli were 500 and 2000 Hz AM tones. Contra lateral noise was white noise, low-pass filtered at 700 and 4000 Hz at the CFs of 500 Hz and 2000 Hz, respectively. The actual noise level was 65 to 69 dB SPL for 0.7-kHz low-pass filtered noise and 70 to 74 dB SPL for 4-kHz low-pass filtered noise. The effect of contra lateral noise on the amplitudes and average thresholds of the 40- and the 80- Hz ASSR at the two CFs was assessed. The study clearly showed that contra lateral noise caused significant threshold elevation (average 10 to 15 dB) and amplitude reduction of the 40-Hz ASSR, with no significant effect on the threshold and amplitude of the 80-Hz ASSR.

Maki et al (2009) explained the differences in the effect of contra lateral noise on the 40- and 80-Hz ASSRs by the locations of the major sources. The 40-Hz ASSR contains more components from the upper auditory pathway that are affected by contralateral masking, whereas the 80-Hz ASSR contains more components from the brain stem. This is consistant with the results of the study of Galambos and Makeig (1992) that the contralateral noise-masking effect occurs in the upper level of the auditory pathway rather than the inferior colliculus. [164, 180] So, they thought that the suppression induced by contralateral noise that was observed only in the 40-Hz ASSR but not in the 80-Hz ASSR, is caused mainly by the central masking mechanism rather than peripheral mechanism.

Recently, by using Magnetoencephalography (MEG) recording of auditory evoked fields, two studies were done, investigating the effect of contralateral noise on 40- Hz ASSR and N100 response [165], and the effect of contralateral noise on 20- Hz ASSR and 40-ASSR. [167] The first one showed that the 40-Hz ASSR is suppressed by contralateral continuous white noise without significant change of the N100 response, although they are both cortical responses. The authors attributed this finding to their different sources in the auditory cortex. Moreover, any type of contralateral sound appears to suppress the 40-Hz ASSR, [12, 164, 166, 180, 181] unlike the N100 response that is suppressed contralaterally by complex stimuli such as pass-band or stop-band and comb-filter noise. [182] The second study also showed that significant suppression of ASSR was occurred by contralateral continuous white noise, with greatest suppression in 40-Hz potential.[167]

A disruption in neural function in patients with ANSD is further indicated by the lack of an olivocochlear reflex (OCR), as demonstrated by absence of contralateral suppression of transient-evoked otoacoustic emissions (TEOAEs). [183]

Hood et al (2003) compared OCR characteristics in patients with ANSD to matched control subjects via suppression effects on TEOAEs measured using binaural, ipsilateral, and contralateral suppressor noise. [10] Ten subjects with documented ANSD, were compared to control subjects matched for age and gender, and had normal hearing thresholds. The results demonstrated significantly reduced suppression of TEOAEs for binaural, ipsilateral, and contralateral suppressor stimulus conditions; suggests an overall dysfunction of the OCR, regardless of the suppressor stimulation paradigm.

In 2000, Abdala et al studied the suppression of distortion product otoacoustic emissions (DPOAEs) and TEOAEs in four subjects with ANSD. [184] The amplitudes of DPOAEs and TEOAEs after introducing 60 dB SPL broad band noise to the contralateral ear, were compared to the amplitudes of the two responses resulted from the same experiment, but in normal hearing control subjects. The result of the study was, neither DPOAEs nor TEOAEs had significant suppression.

The entire auditory pathway is active during the measurement of the ASSRs, but the location of the highest activity seems to vary according to the modulation frequency. The 40-Hz ASSR contains more components from the upper auditory pathway and shows contralateral suppression by contralateral masking signal, whereas the 80-Hz ASSR contains more components from the brain stem and does not show significant suppression, when the two potentials are recorded in normal subjects. The difference in the effect of the contralateral noise on the 40- and 80-Hz ASSRs seems to be related to the difference in the locations of the major sources. This is explained by the hypothesis that contralateral noise-masking effect occurs in the upper level of the auditory pathway rather than the inferior colliculus.

In patients with ANSD, the 80 Hz potential recording showed the same result of the normal listeners, no significant suppression. The 40 Hz potential did not show clinically significant suppression opposite to the results of the normal subjects. The question is, why the patients with ANSD lack contralateral suppression of 40 Hz ASSR ?

The contralateral masking is thought to occur at the cortical level of the auditory pathway during auditory processing. The central masking posits a mechanism of overlapping excitation between contralateral signals at some points in the CNS, and it is

assumed that this phenomenon is mediated by the efferent system, especially by the medial olivocochlear bundle (MOCB). Physiological findings revealed that efferent system function in the form of OCR that mediated by MOCB, provides a mechanism for central feedback to control the activity of the auditory periphery. So, in order to suppress the peripheral system, the auditory cortex needs intact efferent system to convey inhibitory signals to the cochlea to cause suppression.

In ANSD, the efferent system is impaired and those patients characteristically show an abnormal OCR measured by absence of contralateral suppression of OAEs.

The impaired efferent system did not convey the inhibitory signals from the cortex where the central masking occurred, to the OHCs in the cochlea to cause suppression.

Consequently, no significant suppression at 40 Hz ASSR could be detected.

SUMMARY

The current study investigated the effect of contralateral masking noise on hearing thresholds of 40 Hz and 80 Hz ASSR at two CFs, 500 Hz and 4000 Hz, in patients with ANSD.

Several studies investigated the effect of contralateral masking on 40 Hz, 80 Hz ASSR and other evoked potentials as ABR, N100 and 20 Hz ASSR in normal hearing individuals. The results of all studies showed significant contralateral suppression of 40 Hz ASSR-with different types of masker signals-and less suppression of 20 Hz ASSR, with no suppression of ABR or N100. The authors suggested that the suppression occurred by the central masking effect.

The current study was conducted on ten adult participants (20 ears) diagnosed with ANSD, ranging in age from 15 to 53 years attending the Audiology Unit, E.N.T. Department, Alexandria University Hospital. According to the degree of hearing loss, they were selected as to have mild and moderate degree of hearing loss. Five subjects (10 ears) had mild SNHL and five subjects (10 ears) had moderate SNHL. Single channel monotic ASSR was carried out using GSI AUDERA evoked potential system. Two frequencies (500 and 4000 Hz) at 40Hz and 80 Hz were evaluated with and without contralateral BBN of 70 dBHL in intensity. Comparisons between right and left ear, and patients with mild and moderate degree regarding the amount of suppression (difference between before and after noise) were done. Also, thresholds of hearing before and after noise were compared.

It was found that, first; neither overlap of the efferent pathways of both cochleae nor degree of hearing loss -up to moderate- had impact on suppression process. Second, contralateral masking caused statistically significant suppression, but not clinically significant suppreesion neither for 40 Hz nor 80 Hz potential because clinically significant suppression needs high level of threshold elevation to be considered (10 to 15 dB).

Contralateral suppression occurred through central masking mechanism in the auditory cortex, but the inhibitory signals could not be transmitted to the peripheral system through MOC fibers, to cause clinically significant suppression due to affected efferent system in those patients, as it is diagnosed in previous studies that showed the lack of contralateral suppression of OAEs.

The findings of the present study indicated that patients with ANSD lack contralateral suppression of 40 Hz and 80 Hz ASSR as they lack suppression of OAEs due to disordered efferent pathway.