Characteristics of Auditory Brainstem Response Latencies in Children with Autism Spectrum Disorders.

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Introduction

- Autism spectrum disorders (ASD) are complex neuro-developmental disorders, characterized by social and communication impairments and rigid and repetitive behaviours (APA, 2000; WHO,1993).

- **One of the most commonly reported challenges and the most prominent auditory symptoms for people with ASD is hypersensitivity to loudness of sound with abnormal behavioural reactions to environmental sounds *(Frith & Baron-Cohen, 1987; Khalfa et al., 2004).***

- **Stiegler & Davis, (2011) suggested that audiologists assess loudness discomfort levels as part of the routine audiologic assessment protocol for individuals with ASD, or when ASD are suspected.**

- **In infancy and early childhood, it is difficult to obtain reliable subjective responses regarding the true uncomfortable loudness level, and in ASD, it is impossible due to lack of communication.**
- **So using ABR wave V latency intensity function curve, we can objectively get an idea about the loudness growth. Furthermore, ABR has been widely studied in autism, but yielded different results in different studies.**

Aim of Work

- The assessment of any abnormality in the loudness growth objectively using auditory brainstem response (ABR), as well as to study the ABR latency characteristics in normal hearing autistic infants with delayed language development.

SUBJECTS AND METHODS

SUBJECTS

50 children: (*1yr & 6 months - 3yrs & 3months*):

- **25 ASD, 16 males and 9 females**
  - **mean age : 27.52 $\pm$ 6.06 (range 18 - 39) months**
    - Diagnosis made by pediatricians, paediatric psychiatrists, and psychologists.
    - Referred for hearing assessment for their delayed language development.
    - All had intolerance to noise (reported by parents).
    - Those with normal hearing thresholds using auditory brainstem response (20 dB nHL or better) were included.
- **25 controls, 17 males and 8 females**
  - **mean age : 29.48 $\pm$ 5.28 (range 19 - 40) months.**
    - Healthy, without any psychiatric or medical disorders.

Methods:

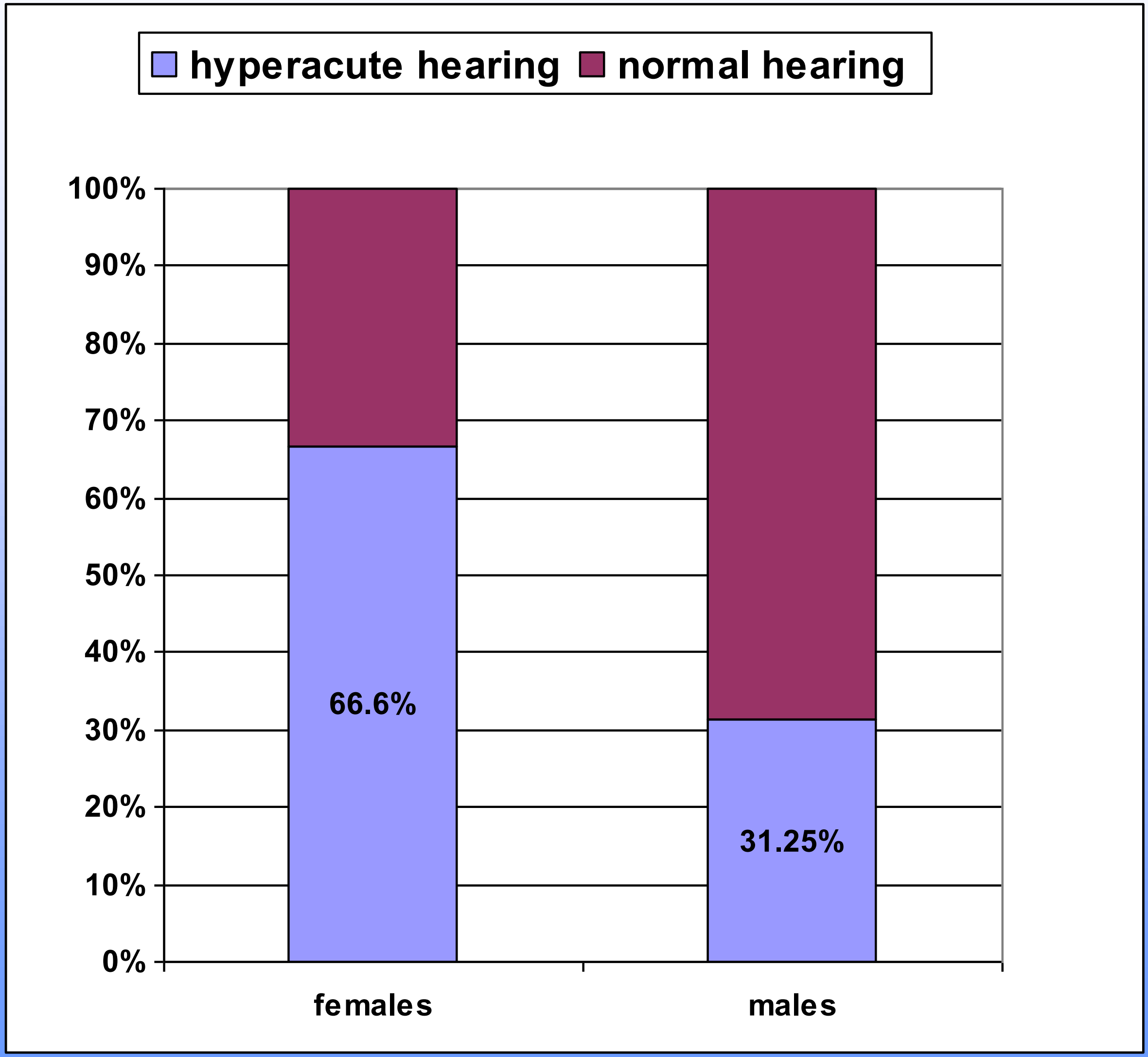
- Full history taking from the parents,
- Otological examination
- Auditory brainstem response (ABR).
- Tympanometry and acoustic reflex threshold.

Results and Discussion

- All three ABR waves were obtained in all cases and controls with clear morphology.

- The electro-physiological hearing threshold
  - for the controls was 20 dB nHL,
  - Eleven /25 (44%) of the autism group showed a lower threshold than their controls, i.e. hyperacute hearing, i.e. true hyperacusis.
    - 5/25 (20%) : hearing threshold of 10 dB nHL
    - 6/25 (24%) : threshold of 0 dB nHL

Figure 1: Electro-physiological hearing threshold



- **In comparison, Rosenhall et al. (1999) noted that 18% of subjects with ASD presented normal auditory thresholds and auditory hypersensibility with intolerance to clicks above 70 dB nHL, when submitted to brainstem audiometry.**
- **Gomes et al. (2005) stated that adverse reactions to sound in individuals with ASD may not reflect a physiological difference in the auditory system, but rather a psycho-emotional-behavioural difference: a fear of sound stimuli, accompanied by hyper-reactive avoidance behaviours.**

Figure 1: ABR traces for autistic and a control child.

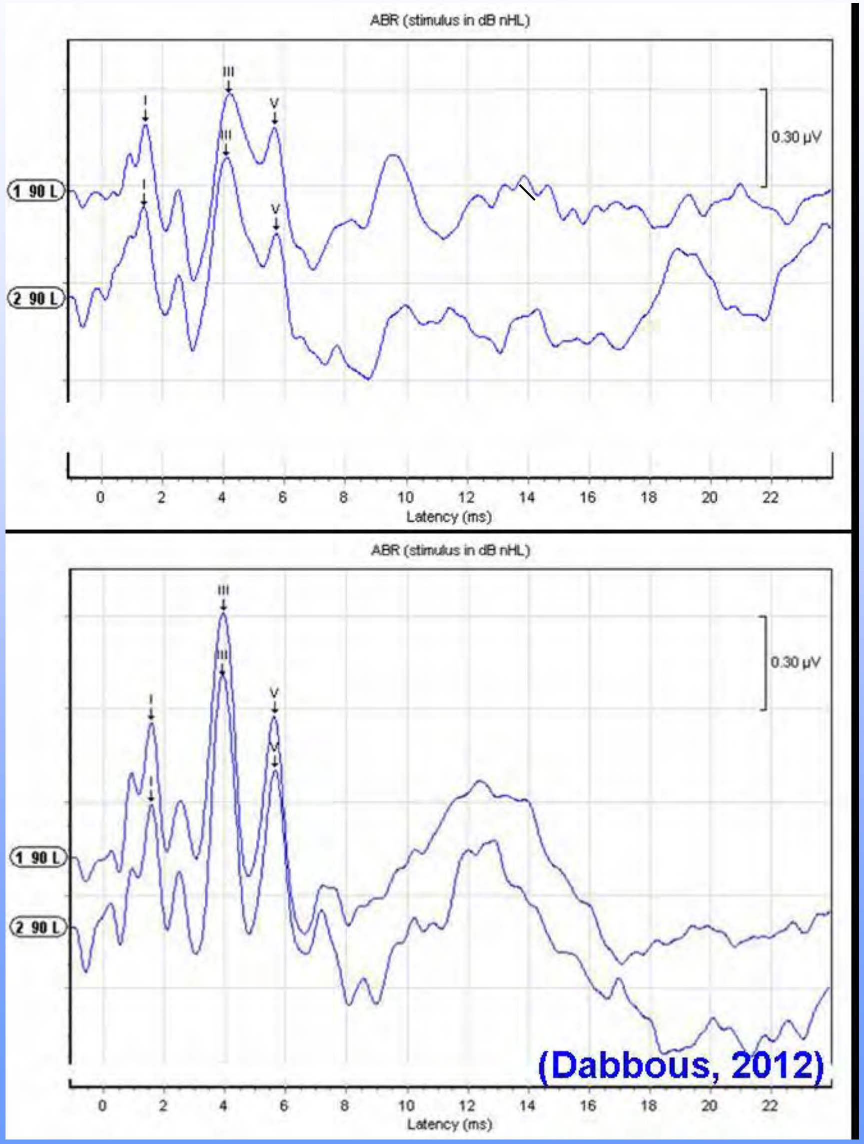


Table 1: ABR Latency Values For Autistic And Control Children

ABR*	Autistic children (n=25)		Controls (n=25)		t-value	p-value
	Mean	SD	Mean	SD		
Wave I	1.39	0.10	1.51	0.10	-4.559	0.000
Wave III	3.91	0.19	3.80	0.13	2.485	0.016
Wave V	5.52	0.20	5.55	0.13	-0.617	0.540
IPI: I - III	2.52	0.16	2.28	0.19	4.831	0.000
IPI: I - V	4.14	0.15	4.04	0.20	1.954	0.057
IPI: III - V	1.61	0.18	1.76	0.12	-3.430	0.001

ABR = auditory brainstem response;
** at 90dBnHL;*
IPI: inter-peak interval.
significantly different at $p<0.05$

- **The significantly earlier autistic children ABR wave I than the controls indicate quicker synaptic processes in the organ of Corti.**

- Coutinho et al. (2002) documented ABR findings showing a prevalent peak I over peak III and peak V in the four ears of two autistic children. They did not find any inter-peak latency abnormalities, and the latencies of peaks I, III and V were within the average range in both cases. They stated that these findings in the ABR could not be related to the unusual responses to auditory stimuli, which are often typical of children with autistic disorder.

- **The prolonged wave III and longer IPI: I- III reflects a retro-cochlear dysfunction in ASD that may be related to their difficulty discriminating, leading to difficulty communicating with others, and at the same time a normal peripheral auditory function that can hear the meaningless sounds which may be related to their abnormal reactions to sounds.**

- Prolongation of wave III latency in children with autism were also reported by Magliaro et al. (2010) and prolongation I – III IPI by Magliaro et al. (2010), Maziade et al. (2000) and Wong and Wong (1991).

- Furthermore, Maziade et al. (2010) observed the same I - III IPL prolongation in the unaffected first degree relatives of the autistic probands compared with controls, which is a sign of retro-ochlear involvement indicating the presence of a slowing in nerve conduction in the auditory system.

- However, Kwon et al. (2007), Magliaro et al. (2010), Rosenhall et al. (2003), and Wong and Wong (1991), found an increase in absolute latencies of wave V and inter-peak I-V and III - V in those with autism compared to controls. This indicate that children with ASD have a dysfunction or immaturity of the central auditory nervous system.

- Kwon et al. (2007) suggested that any children with prolonged III - V IPI, especially high functioning children, should be further evaluated for central auditory processing in order to set up a more appropriate treatment plan.

- But, Tharpe et al. (2006) did not find any differences in central transmission latencies in children with autism compared to their controls.

- Prolongation of waves III and V and IPI I-III and I-V suggested that individuals with autism have a delay in the conduction of the acoustic stimulus at the low brainstem region, which was the most frequent type of alteration (83.3%) and considered statistically significant compared to the high brainstem region (0%), and both (16.7%) (Magliaro et al. 2010).

- Lengthening of the latency of wave V might reflect brainstem abnormality when combined with abnormal IPLs and/or in the presence of normal latencies of the earlier waves was observed in 37% of their cases. This supported the 'brainstem hypothesis ' (Rosenhall et al. 2003).

- Roth et al. (2012) found that all absolute latencies and IPLs were significantly prolonged in the group with suspected ASD compared with the group with language delay, excluding IPL III-V, and compared with clinical norms. And significant prolongation of absolute and IPLs was also evident in the group with language delay compared with clinical norms, excluding IPL III-V.

- This provided first-time evidence for a neuro-developmental brainstem abnormality that is already apparent in young children with suspected ASD and language delay. The overlap in ABR findings supports the assertion that an auditory processing deficit may be at the core of these two disorders (Roth et al. 2012)

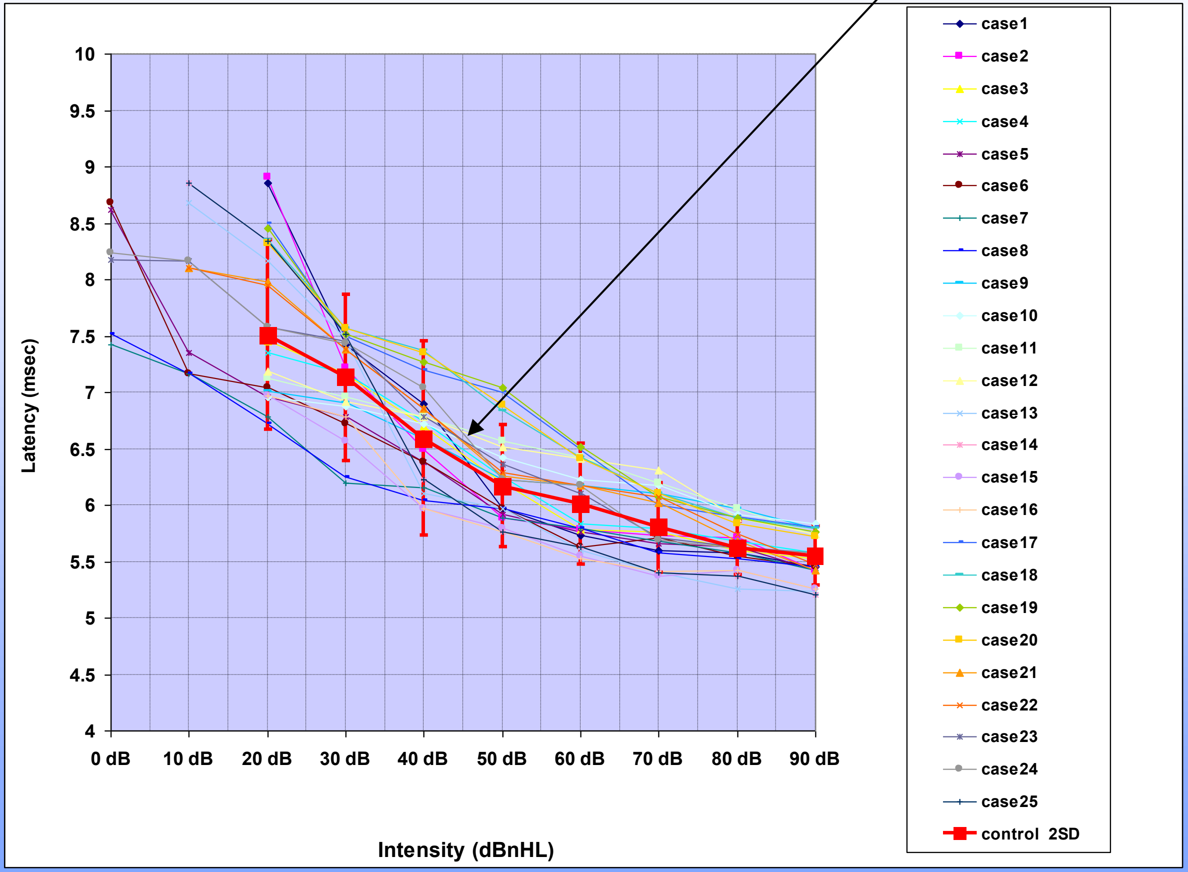
- Aberrant functioning of auditory and auditory association regions would also have potential downstream effects on auditory brainstem regions via cortico-fugal and medial olivo-cochlear efferents (Palmer et al., 2007; Perrot et al, 2006 ; Zhang and Suga, 2000), ultimately affecting early encoding of auditory information (O ’ Connor , 2012).

- So, brainstem lesion, occult cochlear dys-function and involvement of the cochlear efferent system, are probable factors that can explain the ABR abnormalities (Rosenhall et al. 2003).

- In this study there was no abnormal inter-aural latency difference in waves (i.e. ear side differences). This agreed with Fujikawa-Brooks et al. (2010) when a slower presentation rate was used, but they found that fast ABR click presentation rate resulted in significant prolongation of wave V latency, particularly in the right ear.

- In comparison, Kwon et al. (2007) observed that children with ASD in their study seem to have a left ear advantage (shorter wave I, III, and V latency values) than those of the right, but not statistically significant.

Figure 5: Wave V latency-intensity graph of the cases compared to the controls 2 ± SD.

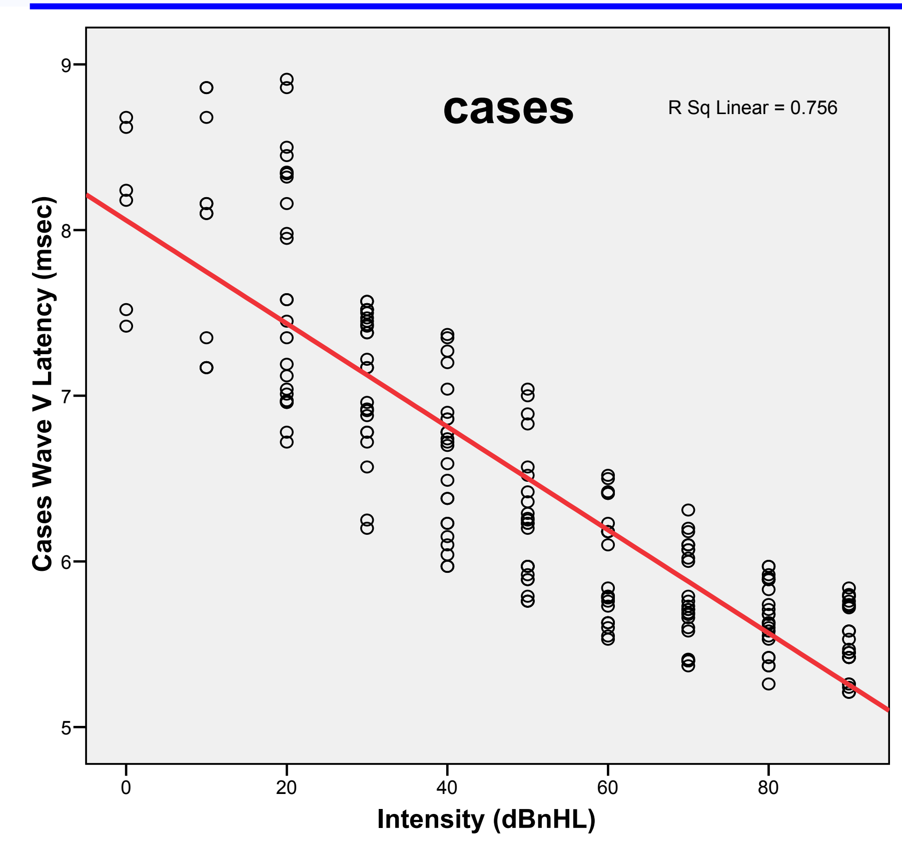


- This reflects a normal loudness growth in the autistic group

Table 2: ABR Wave V latency values at different click levels for autistic and control children.

Wave V at different click levels	Autistic children (n=25)		Controls (n=25)		t-value	p-value
	Mean	SD	Mean	SD		
90 dB	5.52	0.2	5.55	0.13	-0.617	0.540
80 dB	5.67	0.2	5.62	0.12	0.976	0.334
70 dB	5.8	0.29	5.8	0.2	-0.017	0.987
60 dB	5.99	0.34	6.01	0.27	-0.226	0.823
50 dB	6.23	0.4	6.17	0.27	0.608	0.546
40 dB	6.64	0.43	6.59	0.43	0.372	0.712
30 dB	7.13	0.41	7.13	0.37	-0.032	0.974
20 dB	7.67	0.7	7.51	0.42	0.980	0.332
10 dB	7.98	0.67	.	.	.	.
0 dB	8.11	0.53	.	.	.	.

Figure 3: Linear regression analyses of the ABR wave V latency-intensity graph.



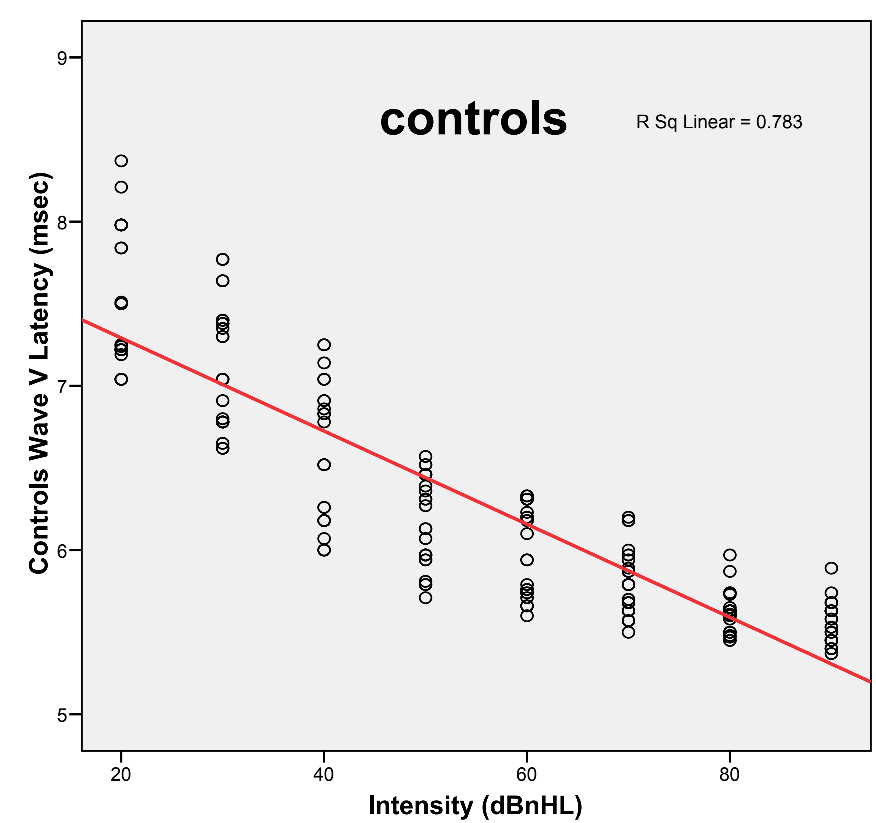


Table 3: ABR Wave V latency -intensity function slope values for autistic and control children.

	ASD (n=25)	Controls (n=25)
Mean of the whole group	-0.030	-0.028
SD	0.011	0.005
SE	0.002	0.001
t value	-0.936	
p value	0.354	

Figure 4: Mean ± 2 standard deviation of the ABR wave V latency-intensity graph of cases and controls.

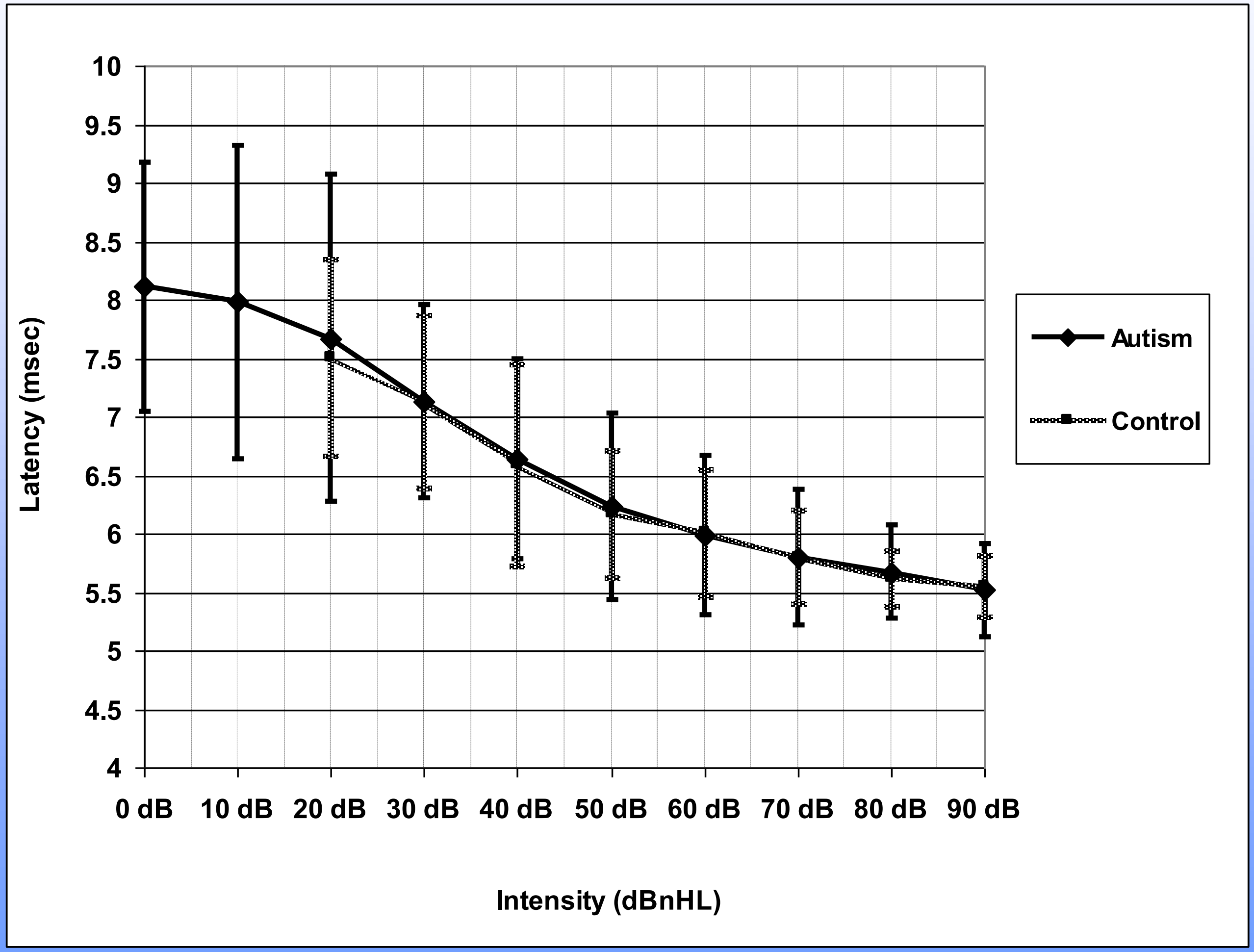


Table 6: ABR absolute latencies of waves and inter-peak latency intervals for male and female autistic children.

ABR	Male Autistic children (n=16)		Female Autistic children (n=9)		Z*	p-value
	Mean	SD	Mean	SD		
Wave I	1.40	0.10	1.36	0.09	-0.856	0.392
Wave III	3.97	0.14	3.82	0.25	-1.876	0.061
Wave V	5.57	0.18	5.45	0.23	-1.336	0.182
IPI: I - III	2.56	0.12	2.45	0.21	-1.134	0.257
IPI: I - V	4.16	0.15	4.09	0.15	-1.532	0.126
IPI: III - V	1.60	0.18	1.64	0.18	-0.340	0.734

**: Z of the nonparametric Mann-Whitney and Wilcoxon test*

ABR=auditory brainstem response; IPI: inter-peak interval.

** = significantly different at p<0.05*

Table 7: ABR wave V latency values at different click levels for male and female autistic children.

Wave V at different click levels	Male Autistic children (n=16)		Female Autistic children (n=9)		Z*	p-value
	Mean	SD	Mean	SD		
90 dB	5.57	0.18	5.45	0.23	-1.336	0.182
80 dB	5.71	0.18	5.58	0.24	-1.560	0.119
70 dB	5.87	0.27	5.68	0.29	-1.787	0.074
60 dB	6.10	0.34	5.80	0.25	-2.017	0.044
50 dB	6.36	0.42	5.99	0.21	-2.130	0.033
40 dB	6.83	0.38	6.28	0.25	-3.175	0.001
30 dB	7.31	0.25	6.81	0.46	-2.580	0.010
20 dB	7.93	0.62	7.22	0.60	-2.833	0.005
10 dB (n=5)!	8.28	0.33	7.73	0.81	-1.206	0.228
0 dB (n=6)!!	8.21	0.04	8.06	0.68	0.000	1.000

**: Z of the nonparametric Mann-Whitney and Wilcoxon test*

! Male =3, females =2

!! Male =2, females =4

Table 5: Comparison between autistic and control children with regard to the ABR wave V latency -intensity function slope values of both genders.

	Males		Females		Z	p value
	Mean	SD	Mean	SD		
ASD	-0.034	0.008	-0.025	0.014	-1.842	0.065
Controls	-0.03	0.006	-0.025	0.002	-1.828	0.068

**: Z of the nonparametric Mann-Whitney and Wilcoxon test*

Figure 6: Mean of wave V latency-intensity graph of male and female control and autistic children.

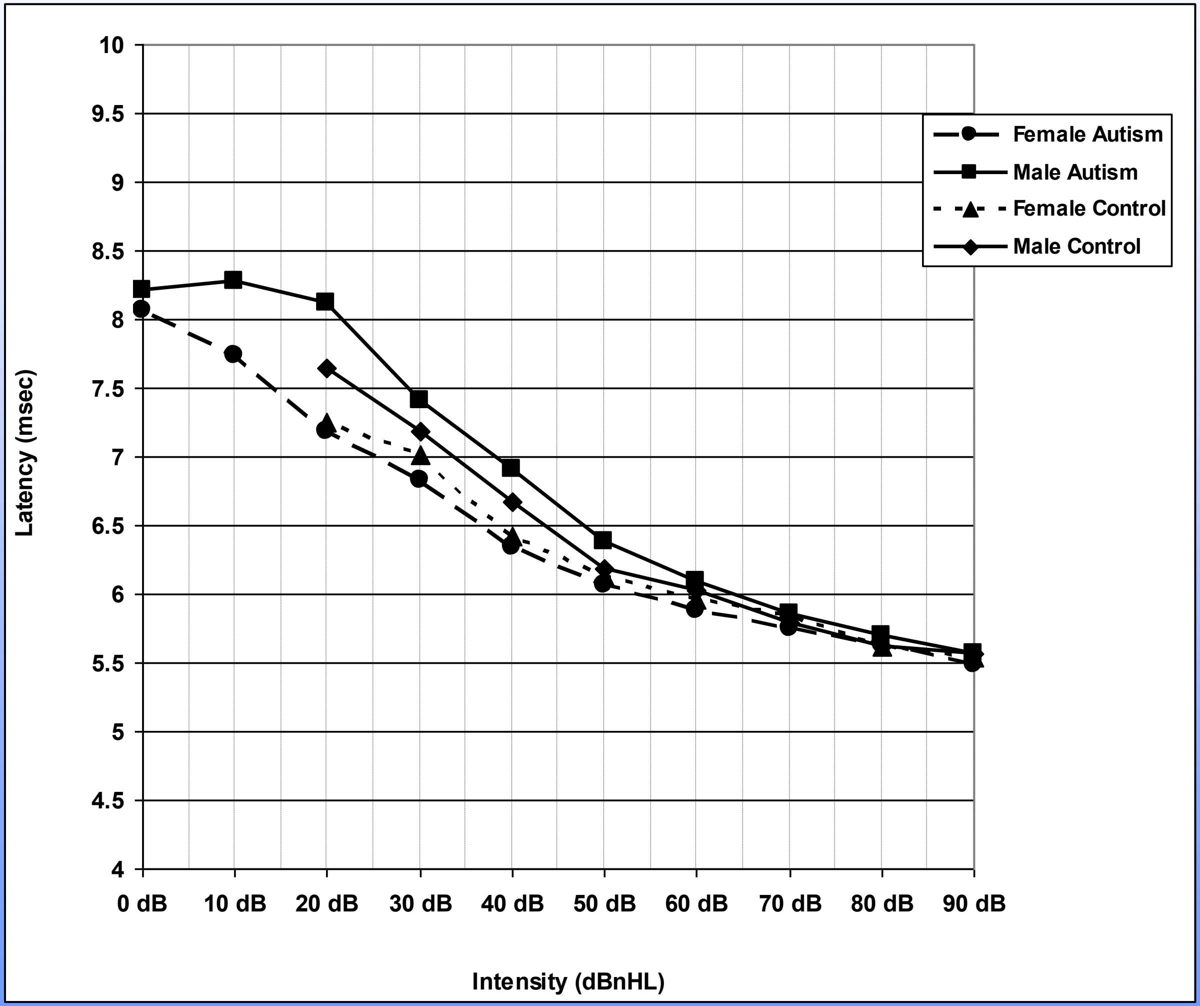


Table 4: Comparison between both genders children with regard to ABR wave v latency -intensity function slope values of autistic and control groups.

	ASD		Controls		Z	p value
	Mean	SD	Mean	SD		
Males	-0.034	0.008	-0.03	0.006	-1.572	0.116
Females	-0.025	0.014	-0.025	0.002	-0.821	0.412

**: Z of the nonparametric Mann-Whitney and Wilcoxon test*

Table 7: ABR wave V latency values at different click levels for male and female autistic children.

Wave V at different click levels	Male Autistic children (n=16)		Female Autistic children (n=9)		Z*	p-value
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60 dB	6.10	0.34	5.80	0.25	-2.017	0.044
50 dB	6.36	0.42	5.99	0.21	-2.130	0.033
40 dB	6.83	0.38	6.28	0.25	-3.175	0.001
30 dB	7.31	0.25	6.81	0.46	-2.580	0.010
20 dB	7.93	0.62	7.22	0.60	-2.833	0.005
10 dB (n=5)!	8.28	0.33	7.73	0.81	-1.206	0.228
0 dB (n=6)!!	8.21	0.04	8.06	0.68	0.000	1.000

**: Z of the nonparametric Mann-Whitney and Wilcoxon test*

! Male =3, females =2

!! Male =2, females =4

- The latency differences in wave V at lower intensity levels between both genders in this study may might reflect the smaller female head size or the lesser amount of soft tissue than in males that may absorb the sound energy.

- This may also reflect slower neural processing in male than female autistic children despite the absence of differences in loudness growth as reflected by the slope of the curve.

- **This, therefore, does not explain the intolerance to sounds that is present in both genders, and may be rather a phonophobic reaction to an external sensory stimulus, or the pathology could be efferent system affection or a more central pathology that needs further evaluation.**
- **However, this may account for the greater frequency of autism in males than females who have near normal processing and that may not easily manifest clinically.**

Conclusion

Conclusion

- Autistic children with normal hearing showed a within normal loudness growth indicating that their abnormal reactions to sounds may either be phonophobia or an efferent system affection or a more central pathology that needs further evaluation. They also showed a retro-cochlear dysfunction that may be related to their difficult communication.


Thank You