AUDITORY BRAINSTEM RESPONSES IN ASPERGER'S SYNDROME*

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SUMMARY

Auditory brainstem responses (ABR) were investigated in six children with Asperger's syndrome and in six normal hearing, healthy children matched for age and sex. There were no statistically significant differences in comparison of latencies of waves I, III, V and interpeak latencies of I-III, III-V, I-V between the two groups (p>0.05). Interaural comparison of these parameters in the Asperger's group yielded no statistically significant differences as well (p>0.05). ABR values two standard deviations beyond the mean were present in the Asperger's group while there was none in the control group. These results indicate that subjects with Asperger's syndrome do not show brainstem dysfunction as the whole group, but when individually evaluated, they reflect a slightly more heterogeneous population than the control group.

Key words: *Asperger's syndrome, auditory brainstem response (ABR)*

ÖZET

Asperger sendromlu altı çocuk ve bu çocuklarla yaş ve cinsiyet açısından eşlemeli, işitmesi normal olan altı sağlıklı çocukta beyinsapı işitsel uyarılmış potansiyelleri (BSİUP) araştırılmıştır. Her iki grup arasında I, III, V. dalgaların latansları ile I-III, III-V ve I-V interpeak latanslarının karşılaştırılmasında istatistiksel açıdan anlamlı fark saptanmamıştır (p >0.05). Asperger grubunda aynı parametrelerin bireylerin her iki kulakları arasında karşılaştırılmasında da istatistiksel açıdan anlamlı fark bulunmamıştır (p>0.05). Asperger grubunda ortalamanın iki standart sapma dışına çıkan BSIUP değerleri olmasına karşın kontrol grubunda bu limitin dışına çıkan değer gözlenmemiştir. Bu sonuçlar grup olarak değerlendirildiklerinde Asperger sendromlu olguların beyinsapı disfonksiyonu göstermediğini ancak bireysel olarak incelendiklerinde kontrol grubuna göre biraz daha heterojen bir popülasyonu yansıttıklarını göstermektedir.

Anahtar sözcükler: *Asperger sendromu, beyinsapı işitsel uyarılmış potansiyelleri (BSİUP).*

The essential features of Asperger's syndrome are severe and sustained impairment in social interaction and the development of restricted, repetitive patterns of behaviour, interests, and activities. The disturbance causes clinically significant impairment in social, occupational, or other important areas of functioning. However it does not cause clinically significant delays in development of language, cognition, age-appropriate self-help skills, adaptive behaviour (other than in social interaction), and curiosity about the environment in childhood (1). Neurobiological nature of the syndrome has been investigated with different neuroimaging studies. Various organic pathologies of the brain have been identified with computed tomographic (CT) and magnetic resonance imaging (MRI) studies (2,3).

Asperger's syndrome has many features in common with autism, the distinguishing factor

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being the presence of delay in language development in autism (1). Besides CT and MRI, auditory brainstem response (ABR) has been widely used in autism to search evidence for the speculation that such behaviours result from distortions in the sensation or perception of environmental stimuli (4-8).

In the present study ABR responses were investigated in Asperger's syndrome in order to evaluate the functional status of the cochlear nerve and auditory pathways of the brainstem. Although having many similarities with autism, to our knowledge an ABR study in Asperger's syndrome was not mentioned before.

MATERIALS and METHODS

Six male subjects with Asperger's syndrome according to DSM IV criteria, ranging in age from 6 to 16 years, and six control subjects matched for age and sex were involved in this study. Axillary temperatures were checked, and all subjects had temperatures below 37°C. Otoscopy, tympanometry and acoustic reflex tests were performed in all subjects. All of them had normal otoscopic findings and tympanograms with positive acoustic reflexes, indicating normal middle ear function. All the subjects in the control group and four of the children in Asperger's group were evaluated with pure tone audiometry and had normal hearing as evidenced by having 20 decibel (dB) hearing level (HL) or better thresholds at each frequency between 250 to 8000 Hz air conduction stimuli. Hearing thresholds in two of the children with Asperger's syndrome were determined with ABR because of the lack of their co-operation for pure tone audiometry. Both of these children had better thresholds than 50 dB peak equivalent pressure level (p.e. SPL): the intensity level which was chosen as the pass/fail criterion for ABR threshold determination. Thus, all the children in both groups showed no hearing impairment with the utilized testing techniques.

After determination of hearing thresholds, ABR recordings were performed in all subjects both in the patient and control groups. Click stimuli presented at 100 dB p.e. SPL intensity with a repetition rate of 11/s was delivered to one ear, and the contralateral ear was masked with 60 dB SPL wide band white noise. The electrical activity was recorded between a positive vertex electrode and a negative mastoid electrode. Forehead was used for placement of the ground electrode. Two thousand artefact free trials for each ear were recorded two times and stored for analysis. Latencies of waves I, III, V and interpeak latencies of I-III, III-V and I-V for both ears in each group were analysed.

Values obtained from the patient group were compared separately for each ear with the control group. Comparison of the right and left ear responses (interaural comparison) was also made in Asperger's group. Statistical analysis of the results of both groups and right-left ear responses of the Asperger's syndrome group was performed using the Mann-Whitney U Test. ABR values 2, 2.58 and 3 standard deviations beyond the mean were also investigated in both groups.

RESULTS

Values of wave I, III, V latencies and I-III, III-V, I-V interpeak latencies for each subject in Asperger's group is demonstrated in Table I, and the control group in Table II.

Comparison of wave I, III, V latencies and I-III, III-V, I-V interpeak latencies between Asperger's group and the control group yielded no statistically significant differences with p values being above 0.05 (Table III).

Interaural comparison of these parameters in Asperger's syndrome group did not show statistically significant differences either (Table IV).

There was no ABR value 3 standard deviations beyond the mean in both groups. ABR values 2 and 2.58 standard deviations beyond the mean were present in Asperger's group, but not in the control group. Outlying values were seen as prolongations in wave I latency and both as prolongations and shortenings in I-V interpeak latency (Table V).

Table I: Latency and interpeak latency values of Asperger's syndrome group

	Right Ear						Left Ear					
Subject number	1	2	3	4	5	6	1	2	3	4	5	6
Wave I latency	1.64	1.68	1.72	1.80	1.80	1.76	1.60	1.60	1.64	1.76	1.84	1.60
Wave III latency	3.88	3.76	3.76	3.72	3.96	3.76	4.00	3.72	3.80	3.76	3.96	3.72
Wave V latency	5.84	5.68	5.64	5.44	5.88	5.48	5.88	5.80	5.64	5.52	5.80	5.56
I-III interpeak latency	2.24	2.08	2.04	1.92	2.16	2.00	2.40	2.12	2.16	2.00	2.12	2.12
III-V interpeak latency	1.96	1.92	1.88	1.72	1.92	1.72	1.88	2.08	1.84	1.76	1.84	1.84
I-V interpeak latency	4.20	4.00	3.92	3.64	4.08	3.72	4.28	4.20	4.00	3.76	3.96	3.96

*All measurement values are in milliseconds

Table II: Latency and interpeak latency values of the control group

	Right Ear						Left Ear					
Subject number	1	2	3	4	5	6	1	2	3	4	5	6
Wave I latency	1.68	1.60	1.56	1.76	1.64	1.68	1.68	1.60	1.52	1.76	1.68	1.64
Wave III latency	3.58	3.80	3.44	4.00	3.76	4.00	3.72	3.84	3.52	3.80	3.72	4.04
Wave V latency	5.56	5.76	5.52	5.88	5.52	5.56	5.64	5.76	5.48	5.60	5.60	5.68
I-III interpeak latency	1.90	2.20	1.88	2.20	2.12	2.32	2.04	2.24	2.00	2.04	2.04	2.40
III-V interpeak latency	1.98	1.96	2.08	1.88	1.76	1.56	1.92	1.92	1.96	1.80	1.88	1.64
I-V interpeak latency	3.88	4.16	3.96	4.08	3.88	3.88	3.96	4.16	3.96	3.84	3.92	4.04

*All measurement values are in milliseconds

Table III: Mean latencies and interpeak latencies for Asperger's and control groups with corresponding p values.

Parameter	Right Ear			Left Ear		
	Mean value (ms)		p value	Mean value (ms)		p value
	Asperger's group	Control group		Asperger's group	Control group	
Wave I latency	1.7333	1.6533	0.0745	1.6733	1.6467	0.9347
Wave III latency	3.8067	3.7633	0.9349	3.8267	3.7733	0.6831
Wave V latency	5.6600	5.6333	0.9358	5.7000	5.6267	0.3760
I-III interpeak latency	2.0733	2.1033	0.7483	2.1533	2.1267	0.5144
III-V interpeak latency	1.8533	1.8700	0.5189	1.8733	1.8533	0.6858
I-V interpeak latency	3.9267	3.9733	0.9356	4.0267	3.9800	0.5144

*(ms): milliseconds

Table IV: Interaural comparison of latency and interpeak latency values in Asperger's group with corresponding p values.

Parameter	Mean value (ms)		p value
	Right ear	Left ear	
Wave I latency	1.7333	1.6733	0.1946
Wave III latency	3.8067	3.8267	0.8693
Wave V latency	5.6600	5.7000	0.7475
I-III interpeak latency	2.0733	2.1533	0.3315
III-V interpeak latency	1.8533	1.8733	0.8079
I-V interpeak latency	3.9267	4.0267	0.4209

*(ms): milliseconds

Table V: ABR values 2 standard deviations beyond the mean

	Parameter	Asperger's group	Control group
RIGHT EAR	Wave I latency	2.10 SD prolongations (Subjects 4 and 5)	-
	Wave III latency	-	-
	Wave V latency	-	-
	I-III interpeak latency	-	-
	III-V interpeak latency	-	-
	I-V interpeak latency	2.77 and 2.10 SD shortenings (Subjects 4 and 6)	-
LEFT EAR	Wave I latency	2.37 SD prolongation (Subject 5)	-
	Wave III latency	-	-
	Wave V latency	-	-
	I-III interpeak latency	-	-
	III-V interpeak latency	-	-
	I-V interpeak latency	2.74 and 2.01 SD shortenings (Subjects 1 and 2)	-

*SD: Standard deviation

DISCUSSION

Asperger's syndrome, which is principally an autistic disorder, has many clinical features in common with acquired right hemisphere dysfunction and has been postulated to result from a developmental abnormality of the right hemisphere. Right hemisphere abnormality and cerebellar abnormalities have been reported on single photon emission computed tomographic (SPECT) imaging in three patients (3). In one subject CT and MRI also revealed enlargement of the right lateral ventricle reflecting a mild degree of right hemisphere atrophy. Neuro-ophtalmologic findings including colobomatous defects involving the optic discs, prepapillary retina and abnormal ocular motility have also been reported (9).

ABR has been extensively used in order to investigate the neurobiological nature of autism. While some studies have found prolongation of wave I latency implying peripheral hearing impairment (10,11), others have not supported this finding (5,12,13). Investigations which found normal wave I latency mostly focused on latencies of wave III, V and on brainstem transmission times reflected by interpeak latencies. Various abnormalities have been reported in these articles (5,6,8,12,13). Also

while some investigators have reported more ABR abnormalities in stimulation of the left ear (5), others have not supported this finding (4,6,7). After the first half of 1980's, articles reporting normal ABR results in autism began to dominate (4,7,14). It is known that sex has an influence on ABR results (15,16). Although it is accepted that age does not influence ABR results beyond 18 months of age, there are also investigations pointing out its effect, especially on peripheral waves (16). The shift of ABR results from abnormal to normal most probably resulted due to exclusion of cases with obvious neurological diseases and better matching of the autistic group with the control group for age and sex. Today it is generally accepted that children with autistic disorder have normal ABR results (17). However, there are exceptions against this survey with later investigations reporting abnormal ABR findings (8,18).

In the present study, in comparison of ABR wave latencies and interpeak latencies, we have not found any statistically significant differences between Asperger's and control groups. Interaural comparison in Asperger's group yielded no statistically significant differences as well. As we were not able to find any investigation about ABR in Asperger's syndrome it was not possible to compare our results with such a group. When compared with autistic children, our results are similar to the literature indicating normal brainstem responses and no interaural differences in the autistic group (4,7,14). This may also be the result of good matching of both groups for age and sex.

When evaluated individually, no subject had ABR values 3 standard deviations beyond the mean in both groups. A cut-off point of 2.58 standard deviations is preferred to define the normal population in some investigations (6,11). When this value was chosen as the limit, two cases of I-V interpeak latency shortenings were observed. When the limit was being further reduced to 2 standard deviations, seven outlying values were seen in Asperger's group while there was still no value beyond this limit in the control group. There were three cases of wave I latency prolongations, two with left ear and one with right ear stimulation. There were also four cases of wave I-V interpeak latency shortenings, two with right ear and two with left ear stimulation. As all the subjects with Asperger's syndrome had normal hearing thresholds and tympanograms, wave I prolongation can not be assumed to result from hearing impairment. Down's syndrome, epilepsy and an increase in temperature are known to shorten I-V interval (15,19,20). As all the subjects had axillary temperatures below 37°C and had neither epilepsy nor Down's syndrome, shortening of this interval can not be explained with these factors. Findings of the present study were similar to other investigations showing both prolongations and shortenings in wave latencies and interpeak latencies in autism on an individual basis (10,13). They were however contrary to investigations showing only prolongations of these parameters (5,6,16,18).

In conclusion, children with Asperger's syndrome had normal ABR results when

evaluated as a group. However when individually evaluated they represented a slightly more heterogeneous population than children in the control group. We think that future investigations with ABR in Asperger's syndrome would be valuable to expand our understanding about the neurobiological nature of this disease.

REFERENCES

1. Diagnostic and Statistical Manual of Mental Disorders, Fourth edition. Washington, DC, American Psychiatric Association, 1994; 65-78.
2. Jones PB, Kerwin RW. Left temporal lobe damage in Asperger's syndrome. Br J Psychiatry 1990; 156: 570-572.
3. McKelvey JR, Lambert R, Mottron L, Shevell MI. Right hemisphere dysfunction in Asperger's syndrome. J Child Neurol 1995; 10: 310-314.
4. Courchesne E, Courchesne RY, Hicks G, Lincoln AJ. Functioning of the brain-stem auditory pathway in non-retarted autistic individuals. Electroencephalogr Clin Neurophysiol 1985; 61: 491-501.
5. Fein D, Skoff B, Mirsky AF. Clinical correlates of brainstem dysfunction in autistic children. J Autism Dev Disord 1981; 11: 303-315.
6. Gilberg C, Rosenhall U, Johansson E. Auditory brainstem responses in childhood psychosis. J Autism Dev Disord 1983; 13: 181-195.
7. Miral S, İkiz AÖ, Günbay U, Baykara A. Otistik çocuklarda erken ve orta latans işitsel uyarılmış potansiyeller. Çocuk ve Gençlik Ruh Sağlığı Dergisi 1994; 1: 79-86.
8. Thivierge J, Bedard C, Cote R, Maziade M. Brainstem auditory evoked response and subcortical abnormalities in autism. Am J Psychiatry 1990; 147: 1609-1613.
9. Brodsky MC, Barber LG, Lam BL, Merin LM, Edelson S. Neuro-ophtalmologic findings in the Asperger disorder. J Neuroophthalmol 1996; 16: 185-187.
10. Tanguay PE, Edwards RM, Buchwald J, Schwafel J, Allen V. Auditory brainstem evoked responses in autistic children. Arch Gen Psychiatry 1982; 39: 174-180.
11. Skoff BF, Fein D, McNally B, Lucci D, Humes-Bartlo M, Waterhouse L.Brainstem evoked potentials in autism. SPR Abstracts 1986;23; 462.
12. Rosenblum SM, Arick JR, Krug DA, Stubbs EG, Young NB, Pelson RO. Auditory brainstem evoked responses in autistic children. J Autism Dev Disord 1980; 10: 215-225.
13. Rumsey JM, Grimes AM, Pikus AM, Duara R, Ismond DR. Auditory brainstem responses in pervasive developmental disorders. Biol Psychiatry 1984; 19: 1403-1418.
14. Grillon C, Courchesne E, Akshoomoff N. Brainstem and middle latency evoked potentials in autism and developmental language disorder. J Autism Dev Disord 1989; 19: 255-269.
15. Stockard JJ, Stockard JE, Sharbrough FW. Non pathological factors influencing brainstem auditory evoked potentials. Am J EEG Technol 1978; 18: 177-209.
16. Thivierge J, Cote R. Brainstem auditory evoked response: normative values in children. Electroencephalogr Clin Neurophysiol 1990; 77: 309-313.
17. Minshew NJ. Indices of neural function in autism: clinical and biological implications. Pediatrics 1991; 87 (5 Pt 2): 774-780.
18. Wong V, Wong SN. Brainstem auditory evoked potential study in children with autistic disorder. J Autism Dev Disord 1991; 21: 329-340.

19. Rodin E, Chayasirisobhon S, Klutke G. Brainstem auditory evoked potential recording in patients with epilepsy. Clin Electroencephalog 1982; 13: 154-161.

20. Sersen EA, Heaney G, Clausen R, Belser R, Rainbow S. Brainstem auditory evoked responses with and without sedation in autism and Down's syndrome. Biol Psychiatry 1990;27:834-840.