Evaluation of Auditory Attention and Memory Skills in Autistic Children after Hyperbaric O2 Treatment

Original Article

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ABSTRACT

Introduction: The children with autism often exhibit abnormalities in auditory central processing including both auditory attention and auditory memory.

Objective: The aim of this research was to determine the effectiveness of the hyperbaric oxygen therapy in improving auditory attention and auditory memory.

Method: The study included 20 children with autism and 20 normally developed children as the control group. The children with autism were evaluated before and after treatment with hyperbaric oxygen using audirory P300 and MMN to evaluate both auditory attention and auditory memory.

Results: There was a statistically significant difference of the auditory P300 and MMN latencies in the autistic children before and after treatment with hyperbaric oxygen therapy. There was a decrease of the P300 and MMN latencies, after the hyperbaric oxygen therapy.

Conclusion: The children with autism showed improvement in both auditory attention and auditory memory after hyperbaric oxygen therapy.

Key Words: Attention, autistic disorder, cognition, hyperbaric oxygenation, memory.

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INTRODUCTION:

Autism is a pervasive developmental disorder characterized by deficits in socialization, communication, and adaptive functioning with restrictive and repetitive behaviors[1-3]. In addition, children with autism often exhibit abnormalities in auditory processing including both auditory attention and memory[4,5].

Hyperbaric oxygen therapy (HBOT) involves inhaling up to 100% oxygen at a pressure greater than one atmosphere (atm) in a pressurized chamber. HBOT is indicated in several clinical disorders include healing of wounds, diabetic foot[6], arterial gas embolism, decompression sickness and carbon monoxide poisoning[7]. Higher pressure HBOT increases the plasma oxygen content and body tissues and may normalize oxygen levels in ischemic tissue[8].

Hyperbaric oxygen may improve the cerebral hypoperfusion and mitochondrial dysfunction in children with autism, it decreases brain inflammation as well as oxidative stress in autism[9]. Hyperbaric oxygen therapy does not exacerbate the increased oxidative stress in autism. Moreover, it does not affect plasma oxidized glutathione level[10,11].

The use of oxygen appears to enhance neurological function. Oxygen administration in healthy young adults enhances cognitive performance, including improved performance on cognitive function, attention, reaction times, and word recall[12].

Our work was designed to evaluate the improvement of both auditory attention and memory in children with autism after treatment with hyperbaric oxygen, using auditory P300 and mismatch negativity (MMN) tests.

SUBJECTS AND METHOD:

A. Subjects:

This study included 20 children with autism and 20 normally developed children as controls. All participants had normal peripheral hearing evidenced by the audiogram (Fig. 1). This study was conducted in Tanta University hospital between February to October 2017.

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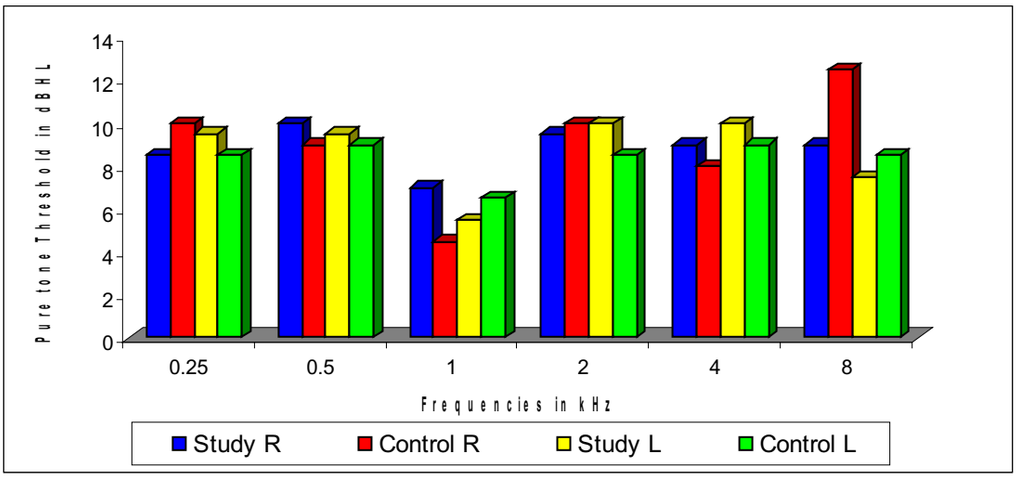

R: right ear, L: left ear

Fig. 1: graph represent pure tone threshold in the control and the study group in right and left ear. It shows normal peripheral hearing in both groups.

The autism group (I) consisted of 20 children of high-functioning autism. Their IQ was more than 70 and Childhood Autism Rating Scale (CARS) less than 33. The study group had attention and memory affection which diagnosed by Stanford Binet intelligence scale-fifth edition cognitive subtest and confirmed by P300 and MMN tests before hyperbaric oxygen therapy. The age of the study group ranged from 8-14 years with the mean of 10.6±2.4. This age group was selected to understand the tests' instructions easier than younger age groups. The control group was chronologically age matched with the study group.

We excluded the children who did not understand the instructions of the tests and children lost in the follow up. We also excluded children suffering from major medical, neurological or psychiatric diseases, abnormal EEG and patients taking drugs that can affect cognitive functions. We excluded cases with persistent dysfunction of the middle ear ventilation (diagnosed clinically and by immittancemetry) as they were contraindicated for the use of HBOT. We excluded children with pneumothorax or emphysema, ruptured tympanic membrane and ejection fraction less than 60% as these are also contraindications of HBOT. On the other hand, the control group (II) consisted of 20 children with no complaint of any cognitive, developmental disorder or history of special education. Normal auditory attention and memory in the control group was confirmed by Stanford Binet intelligence scale-fifth edition cognitive subtest.

The study was approved by the institutional ethics committee in Faculty of Medicine Tanta University and all participants gave informed written consent from their parents before entering the study. All the procedures followed in this study were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 1983.

B. Method

i. Detailed personal and medical history.

ii. Basic audiological evaluation by standard pure tone audiometer GSI version 61 audiometer (Viasys- USA) Flow Sensor for VIASYS AVEA Ventilator, New, Original) for pure tone audiometry using headphone TDH 39. Play audiometry by interacoustics (AD226) was done in some cases that were not cooperative in pure tone audiometry. Acoustic immitance measurements (tympanometry/stapedial reflex) by interacoustics AT235H impedance using low frequency 226 Hz probe tone (Middelfart, Denmark).

iii. Event related potentials (ERPs): elicited by Smart EPs of Intelligent hearing system using ER3A insert phone (HIS, Miami, FL). Electrode montage: high frontal Fz and one low frontal Fpz for positive electrode and ground electrode, respectively. The last two electrodes were placed on the left and right mastoids (as reference electrodes). All electrodes were connected to the pre-amplifier of the Smart EP equipment. The case group was assessed by both P300 and MMN pre and forty sessions post intervention of HBOT while the control group was assessed by both tests with no intervention of HBOT:

a. Auditory P300 was recorded using oddball paradigms where in two tone stimuli were presented in a random order, one occurred less frequently than the other (target: 2000 Hz tone burst with 50 msec rise/fall time and 200 msec plateau.). The child was required to discriminate target (the rare) stimulus

from the frequent one (standard: 1000 Hz tone burst) by counting it. The test instructions were simplified as possible to the children. All the children had undergone training on the test before test recording began to assure that they understand the instructions. The probability of target and standard stimuli were 20 and 80 percent respectively at a rate 0.7/s. The total numbers of stimuli were not less than 100 stimuli and not more than 200 stimuli in each run. Stimuli presented monaurally at an intensity of 80 dBnHL.

Two parameters of P300 were measured (amplitude & latency). The amplitude in microvolt (μv) was defined as being the potential difference between the baseline and the peak of the positive wave. P300 latency was defined in msec as the period of time between the stimulus onsets and the wave apex.

B. Mismatch Negativity (MMN) was recorded using oddball paradigms in response to tone stimuli; 1200 Hz tone burst as a target and 1000 Hz tone burst as a standard. Stimuli presented monaurally at an intensity of 70 dBnHL. Polarity of the stimulation was alternating at a rate 1.1 /s. Probability of the stimuli 85% for the standard and 15% for the target. The children were instructed to lie down calmly and allowed to choose read a story, looking at some interesting pictures or playing with a toy or simple game. At the same time, they were instructed not to concentrate on the presented stimuli.

After finishing the test we detected N100 latency on both standard and deviant traces as the negativity that occur around 100 msec. MMN was calculated in the difference wave form. This was done by creating a new destination buffer. Then the trace that occurred in response to the deviant stimulus alone was added to this new buffer. After that, the trace that occurred in response to standard stimulus alone was subtracted from the response to the deviant stimulus. The resulting difference between the standard and deviant stimulus traces represented the MMN responses which were identified visually as the prominent negativity following N100.

Two parameters of MMN were measured (amplitude & latency). The amplitude in microvolt (μv) was defined as being the potential difference between the baseline and the peak of the negative wave following N100. MMN latency was defined in msec as the period of time between the stimulus onsets and the negative wave apex following N100.

iv. Hyperbaric therapy: (was only applied to the study group) at 1.5 atm and 100% oxygen in a monoplace Sechrist 3600E hyperbaric chamber using Sechrist 3600E hyperbaric chamber for hyperbaric therapy. This therapy was given 45 minutes daily for a total of 40 sessions per child.

Statistics:

Data were analyzed using Statistical Program for Social Science (SPSS) version 20. Quantitative data were expressed as mean± standard deviation (SD).

The following tests were done:

- Independent t test for comparison between control and study groups before hyperbaric oxygen therapy
- Dependent t-test was used for comparing between before and after hyperbaric oxygen therapy in the study group

P-value < 0.05 was considered statistically significant

RESULTS

This study included 40 children with normal peripheral hearing (Fig. 1). Group (I) consisted of 20 children (11 males and 9 females) diagnosed as autistic with attention and memory affection which diagnosed by Stanford Binet intelligence scale-fifth edition cognitive subtest and confirmed by P300 and MMN tests before hyperbaric oxygen therapy.. The control group (II) consisted of 20 children (10 males and 10 females). The age in the study group ranged from 8-14 years with the mean of 10.6±2.4. The age of the children in the control group was chronologically matched with the study group. There were no statistically significant differences as regards sex between the two groups ($p > 0.05$).

There were no statistically significant differences between right and left ears as regard latency and amplitude of both P300 and MMN tests in the both groups ($p > 0.05$). So, both ears were considered as one group including 40 ears in the control and the study group in the following tests.

There were statistically significant differences between both groups ($p < 0.05$) on comparing P300 and MMN latencies and amplitudes before HBOT; the study group showed delayed latencies and decreased amplitudes for both P300 and MMN (Table 1, Fig. 2,3).

There was a statistically significant decrease ($p < 0.05$) in P300 and MMN latencies in the autistic children after treatment with hyperbaric oxygen therapy. Although, the amplitude of P300 and MMN in the study group was increased after hyperbaric oxygen therapy; it was not statistically significant (Table 2, Fig. 2,3).

Table 1: Comparison between P300 and MMN latency and amplitude in the control group and the study group before hyperbaric oxygen therapy

		Group I (patients)	Group II (controls)	T. test	*P-value*
P300 Latency (msec)	Mean ± SD	351.46 ±31.85	325.04± 28.16	3.9	0.0002*
	Range	319:383	301:352		
P300 amplitude(uv)	Mean ± SD	3.16±1.57	4.7±0.94	-5.26	<0.0001*
	Range	1.5:4.7	3.8:5.7		
MMN Latency(msec)	Mean ± SD	239±18.05	205±63.37	3.26	0.0016*
	Range	219:258	135:268		
MMN Amplitude(uv)	Mean ± SD	1.39±0.5	2.01±0.52	-5.43	<0.0001*
	Range	0.9:1.9	1.5:2.6		

*Significant $P < 0.05$

MMN, mismatch negativity; This table shows the comparison between P300 and MMN latency and amplitude in the control group and the study group before hyperbaric oxygen therapy. There were statistically significant differences between both groups; the study group showed delayed latencies and decreased amplitudes for both P300 and MMN.

Table 2: Comparison between P300 and MMN latency and amplitude before and after treatment with hyperbaric oxygen in the study group

		Before HBOT	After HBOT	T. test	*P-value*
P300 Latency (msec)	Mean ± SD	351.46 ±31.85	338.6± 19.61	-2.2	0.033*
	Range	319:383	311:342		
P300 amplitude(uv)	Mean ± SD	3.16±1.57	3.9±1.94	1.9	0.065
	Range	1.5:4.7	2.8:5.4		
MMN Latency(msec)	Mean ± SD	239±18.05	229.6±18.05	-2.33	0.023*
	Range	219:258	209:248		
MMN Amplitude(uv)	Mean ± SD	1.39±0.5	1.59±0.41	1.96	0.054
	Range	0.9:1.9	1.3:2.2		

*Significant $P < 0.05$

MMN, mismatch negativity; This table shows the comparison between P300 and MMN latency and amplitude before and after treatment with hyperbaric oxygen in the study group. There was a statistically significant decrease ($p < 0.05$) in P300 and MMN latencies in the autistic children after treatment with hyperbaric oxygen therapy.

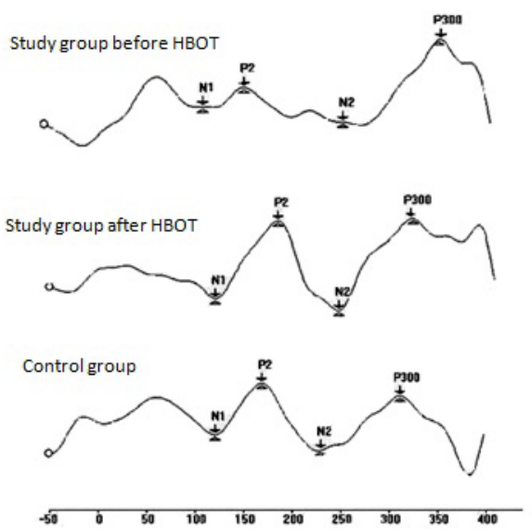

Fig. 2: P300 waves in control group and study group before and after HBOT

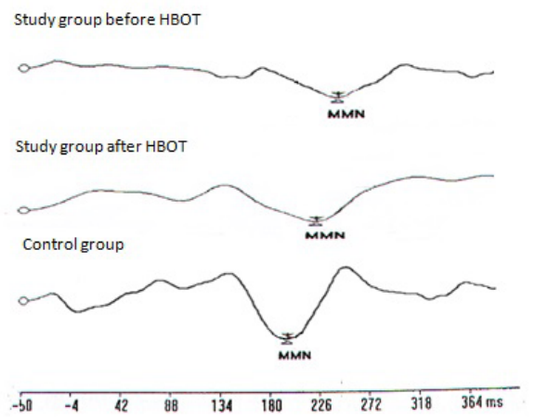

Fig. 3: MMN waves in control group and study group before and after HBOT

DISCUSSION:

Abnormalities in the auditory processing including both auditory attention and memory usually occur in the autistic children[4,5]. Our results showed that the HPOT improved auditory attention and memory in autistic children.

Hyperbaric oxygen treatment (HBOT) is indicated in several clinical disorders include decompression sickness, healing of problem wounds and arterial gas embolism[7]. Stoller[13]. in his study reported a significant improvement in the IQ of a 15 year old child who had a fetal alcohol syndrome using HBOT at 1.5 atm/100% oxygen for 73 sessions. Others[14-17]. had reported that the HBOT possesses a neuro-protective effect, and can enhance the cognitive functions including the attention and memory. The HBOT may improve some physiological abnormalities of the autistic children including the cerebral hypoperfusion, inflammation, and mitochondrial dysfunction[9].

There are scanty of studies searching for the effect of HBOT on autism and there is a debate if the HBOT increase the oxidative stress via the production of reactive oxygen species or not[18]. This may have a special importance especially that some children with autism express evidence of increased oxidative stress including lower serum glutathione levels,[19-21] and decreased the activities of antioxidant enzymes including superoxide dismutase (SOD), glutathione peroxidase,[22] catalase,[23] and paraoxonase (an enzyme that prevents lipid oxidation and also inactivates organophosphate toxins in humans) [24] Some autistic children also demonstrate evidence of increased lipid peroxidation;[23,25,26] this includes increased malondialdehyde which is a marker of oxidative stress and lipid peroxidation.[27] Wada K. *et al*.[28] reported in their study that the oxidative stress can occur with the HBOT but appears to be of a less concern at the hyperbaric pressures under 2.0 atm. On the other hand, other studies[29,30] showed that long-term and repeated administration of the HBOT below 2.0 atm, can actually decreases the oxidative stress by reducing lipid peroxidation,[31] and by up-regulating the activity of antioxidant enzymes including SOD,[29,32] glutathione peroxidase,[33] catalase,[34] and paraoxonase[31,35].

Our results agreed with Heuser *et al*.[36] who reported treatment of a four year old child with autism using the hyperbaric oxygen therapy and noticed improvement in the behavior including the memory and the cognitive functions after ten sessions. This child also had marked improvement of the cerebral hypoperfusion as measured by pre-hyperbaric and post-hyperbaric Single Photon Emission Computed Tomography (SPECT) scans.[37] Shi XY *et al*.[38] reported clinical improvements in six autistic children by the hyperbaric oxygen therapy. Our results agreed with Rossignol *et al*.[10] , they studied the effects of hyperbaric oxygen therapy on oxidative stress, inflammation, and symptoms in children with autism.

From our results, we concluded that HBOT improve auditory attention and memory in cases of autism. We recommend increasing the sample size in the further studies on the effect of hyperbaric oxygen therapy in cases of autism with more number of HBOT sessions.

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NAD

AUTHORSHIP CONTRIBUTION:

All authors included in clinical examination, collecting the data, writing and preparation of manuscript.

CONFLICT OF INTEREST:

None.

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