

SunKrist Journal of Psychiatry and Mental Health

Research Note Volume: 1, Issue: 1 Scientific Knowledge

Cure of Autistic Disorders: Mission Impossible is Possible in an Illustrated Pioneering Experience

Aamir Jalal Al-Mosawi*

¹Advisor in Pediatrics and Pediatric Psychiatry Children Teaching Hospital of Baghdad Medical City

1. Abstract

Background: Autistic disorders have become increasingly known as pervasive developmental disorders since the 1980s. They have been recently called autism spectrum disorder mostly by the American Psychiatric Association. They include five chronic disorders marked by early impairment in socialization, communication and behavior. There is no curative therapy or therapies for autistic disorders and they continue to be regarded as lifelong disorders. The aim of this paper is to describe our extensive experiences with treatment of autistic disorders with emphasis on the possibility of curing these disorders with a new therapeutic approach. improvement or disappearance of autistic features in these disorders has not been reported with any therapy before.

Materials and methods: During the period from December, 2017 to November, 2019, 116 patients with various autistic disorders were observed at the pediatric psychiatry clinic of the Teaching Hospital of Baghdad Medical City. 84 (72.4%) patients were males and 32 (28.6%) female's patients were females. The patients' ages ranged from two years to 16 years. The patients were from several provinces in Iraq including Baghdad, Saladdin, Najaf, Wassit, Kerbalaand Erbil in the North of Iraq).

The patients were reported previously in several

publications. All the patients had very poor speech development except the patients with Asperger syndrome. Most of the patients with a diagnosis other than Asperger syndrome were not saying any word and few patients were saying few words.

Most patients were treated with a new therapeutic approach which included injectable cerebrolysin as the main therapeutic component. Marked improvement or disappearance of autistic features in these disorders has not been reported with any therapy before.

The patients were treated with a new approach which aimed at improving the cardinal features of autistic disorders which include impairment of social interaction which is mostly manifested by poor responsiveness to their name and infrequent engagement with others manifested by poor eye contact and infrequently looking to faces.

It was not possible to follow all the patients regularly nor was it possible to document details of the treatment and responses of all patients.

Results: Almost all the patients treated with the new therapeutic approach experienced some improvement and lessening of the autistic features during the follow-up period. Treatment was also associated with initiation

'Corresponding author: Al-Mosawi AJ, Department of Pediatrics and Pediatric Psychiatry, Children Teaching Hospital of Baghdad Medical City, Iraq, E-mail: almosawiAJ@yahoo.com

Received Date: August 13, 2020; Accepted Date: August 17, 2020; Published Date: August 21, 2020

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²Head, Iraq Headquarter of Copernicus Scientists International Panel Baghdad, Iraq

of speech and improvement of repetitive behaviors. It was possible to document complete disappearance of the main autistic features in twenty patients.

It seems that the patients who achieved complete disappearance of the main autistic features will need an intensive learning especially of speech to abolish the effect of the time when they were under the effect of autistic behavior and to push them toward a possible cure of their illness.

Conclusion: In this paper, we have demonstrated the possibility of cure of autistic disorders including autism and Asperger syndrome with use of individualized courses of intramuscular cerebrolysin as the main therapy for the main autistic features (Impaired social interaction and communication dominated by the lack of response to their name and poor eye contact).

Understanding, a cure of autism will not immediately abolish the cumulative effect of the condition on learning, behavior and speech development before cure.

2. Keywords: Autism; Asperger syndrome; Cerebrolysin; Cure

3. Introduction

Autistic disorders have become increasingly known as pervasive developmental disorders since the 1980s. They include five chronic disorders marked by early impairment in socialization, communication and behavior [1-4]. These disorders were first recognized by Grunya Efimovna Sukhareva in 1925, a Soviet pediatric psychiatrist who called these disorders autistic psychopathy [2,5]. In general, most of manifestations of pervasive developmental disorders result from impairments in social interaction and communication and behavioral problems [1-6].

3.1. General manifestations of pervasive developmental disorders include [1-3]:

Impaired social interaction marked by lack of eye contact, lack of facial responses and not responding to own name appropriately.

Difficulties in using and understanding language.

Unusual patterns of playing with toys and other objects that can be marked by restricted interests.

Repetitive body movements or behavior patterns including hand flapping, hair twirling, foot tapping, spinning, or other complex movements.

The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, 1994) divided pervasive developmental disorders five subgroups [1-3].

Autistic disorder: Autistic disorder is also called classical autism was first described by Leo Kanner in 1943 [3,6].

Asperger syndrome: Asperger syndrome was first described by Grunya Efimovna Sukharevaand later by Hans Asperger in 1944 [3,6].

The autistic psychopathy's described in 1925 by Grunya Efimovna Sukhareva and Hans Asperger were similar and characterized by the absence of significant impairment in language development and cognitive function [3,6].

Lorna Wing was probably the first to use the term Asperger syndrome in the English-speaking medical community in her 1981 publication of a series of case studies of children showing similar symptoms [3,6].

Uta Frith translated Asperger's paper to English in 1991and published it as a book with Cambridge University Press [3,6].

Asperger syndrome has become a standard diagnosis in 1992, when it was included in the tenth edition of the World Health Organization's diagnostic manual, International Classification of Diseases (ICD-10); in 1994, it was added to the fourth edition of the American Psychiatric Association's diagnostic reference, Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [3,6].

The World Health Organization (WHO) defined Asperger syndrome as one of the pervasive developmental disorders or autism spectrum disorders which are a variety of psychiatric conditions that are characterized by impairment of social interaction and nonverbal communication and by restricted and

repetitive interests and behavior [3,6].

Rett disorder: Rett disorder was most probably first described in German language in 1966 by Andreas Rett, a pediatrician in Vienna. Bengt Hagberg, a Swedish pediatrician, published an English article in 1983 and named the condition after Rett [3,6,7].

Childhood disintegrative disorder (Heller syndrome) is a rare heterogeneous clinical syndrome that is distinctive from autism and Asperger syndrome. It is characterized by a significant developmental regression resulting in deterioration in behavioral and adaptive functioning including self-help skills with loss of language and social skills after a period of normal development for at least two years [3,6,8,9]. The condition was first reported in 1908 by Theodor Heller in his paper "Über Dementia Infantilis". He called the condition "Dementia infantilis" [3,6,8,9].

Pervasive developmental disorder not otherwise specified (Atypical autism).

This type reflects the marked variability of these disorders. It may include disorders with well-defined clinical features such as regressive autism and autism with significant mental retardation which seems to be also classifiable under idiopathic mental retardation with significant autistic features [1-3].

Regressive autism is just like Heller syndrome, it is associated with initial normal development followed by loss of the previously acquired skills of socializing, communication and language skills. However, regressive autism is not associated with features of dementia or significant mental retardation [4,6].

Pervasive developmental disorders have recently been called autism spectrum disorder mostly by the American psychiatric association and the term pervasive developmental disorders has been used with the term autism spectrum disorder interchangeably [2-3].

4. Patients and Method

During the period from December, 2017 to November, 2019, 116 patients with various autistic disorders were observed at the pediatric psychiatry clinic of the

Teaching Hospital of Baghdad Medical City. 84 (72.4%) patients were males and 32 (28.6%) female's patients were females. The patients' ages ranged from two years to 16 years. The patients were from several provinces in Iraq including Baghdad, Najaf, Wassit, Kerbala and Erbil in the North of Iraq). The patients were reported previously in several publications [1,7,9-11]. All the patients had very poor speech development except the patients with Asperger syndrome. Most of the patients with a diagnosis other than Asperger syndrome were not saying any word and few patients were saying few words.

Most patients were treated with a new therapeutic approach which included injectable cerebrolysin as the main therapeutic component. Marked improvement or disappearance of autistic features in these disorders has not been reported with any therapy before.

The new approach aimed at improving the cardinal features of autistic disorders which include impairment of social interaction which is mostly manifested by poor responsiveness to their name and infrequent engagement with others manifested by poor eye contact and infrequently looking to faces.

Most patients also required neuroleptics to control hyperactivity and other abnormal behaviors. Trifluoperazine and prochloperazine were used as frequently. Risperidone was also used in some patients when necessary. Some patients also received citicoline as an adjunctive therapy to improve speech development.

It was expected that improving social interaction will contribute to improving other features especially verbal communication and speech.

Courses of intramuscular cerebrolysin were given in individualized regimen depending on the age and severity of the illness and with aim of improving social interactions including response to name, looking at faces and eye contact.

It was not possible to follow all the patients regularly

nor was it possible to document details of the treatment and responses of all patients.



Figure 1A: Patient 1 in the first group of treated patients had moderately severe autistic features, he was looking infrequently to faces and had minimal eye contact and was poorly responding to his name. He was totally unresponsive to the doctor when asked him to take the pen and try to copy a line or just scribble. The mother also failed in making him take the pen to scribble or to draw anything.



Figure 1B: Patient 2 in the first group of treated patients. At the clinic, he had moderately severe autistic features, was looking infrequently to faces and had minimal eye contact and was not responding to his name.



Figure 1C: The third treated patient in the first group was first seen late during April, 2018. At the clinic, he was very hyperactive and not responding to any command. He showed almost no eye contact and was not responding to his name at all. However, it was possible to convince the child by his parents with difficulty to take a pen. He was unable to copy neither a line nor a circle, but he scribbled.



Figure 1D: The treated fourth patient in the first group of patient. At the clinic, he was looking infrequently to faces and had no eye contact and was not responding to his name. He was preoccupied with his toy.



Figure 1E: The treated fifth patient in the first group of patient had Asperger syndrome with milder autistic features. He was neither that cooperative nor responsive and showed minimal eye contact and minimal looking at face. He took the pen but he didn't use it appropriately. However, after some directions from the mother and some time, boy obeyed his mother and started writing and drawing. When his name was called more than one time to bring his attention and asked to look on the O clock on the wall saying "Look at this beautiful O clock on the wall", he looked at the wall. The boy was also responsive to his mother (but not to the doctor), when she asked to make a cheese to take a photo and looked at the camera.



Figure 2A: A six year old boy with typical autism. He had impaired social interaction as he was not responding appropriately to calling his name was showing no eye contact.

The protocol for this research was approved by the

scientific committee of Iraq headquarter of Copernicus Scientists International Panel and conforms to the provisions laid out in the Declaration of Helsinki (as revised in Edinburgh 2000):

www.wma.net/e/policy/b3.htm.



Figure 2B: A seven-year old girl with typical autism, she had impaired social interaction as she was not responding appropriately to her name was showing no eye contact. She also showed frequent repetitive movements.



Figure 2C: An eight-year-old boy with severe autism and had significant behavioral abnormalities. He was not saying any word. At the clinic, he was unable to sit still on the chair without frequently changing the position of his body. He also displayed marked repetitive behavior at the clinic.



Figure 2D: A three-year boy with severe autism which made his parents though him to be deaf, but hearing assessment showed that the boy had normal hearing. At the clinic, before treatment, the boy

was rather uncontrollable and displayed marked repetitive movements in the form of body rocking and was trying to leave the room.



Figure 2E: An eight-year boy with autism who was unable to copy a circle.



Figure 2F: A six-year boy with autism who was unable to copy a circle.



Figure 2G: A five-year old girl with the mildest autism. She accepted the doctor request to take a pen, but she couldn't copy anything. She also had the higher vocabulary of all patients with autism of about 25-30 words and she waved goodbye when the mother asked her to wave goodbye when leaving.



Figure 2H: A boy with severe autism associated with mental retardation that was overweight and his sister had the same condition. At the clinic he was uncontrollably hyperactive and showed marked repetitive movements.



Figure 21: The eight-year old girl with atypical autism which was considered to have the most severe disorder among the patients with typical and atypical mental retardation. She was totally uncontrollable and very irritable.



Figure 2J: A seven-year old girl was considered to have the mildest form among all patients in this series with good language development and response to many requests with the encouragement of the mother. She also welcomed taking a photo with doctor.



Figure 2K: The girl Asperger syndrome and good language development, but she had delayed onset of speech after four years.

She had prominent emotional fluctuation. At the clinic, before treatment she was showing alternating mood, smiling and almost crying with in the same minute and without obvious reason.



Figure 2L: A nine-year boy who was considered normal by the age of four years. The child illness started insidiously with gradual deterioration in speech and cognition, development of abnormal behaviors including motor stereotypies, loss of communication and social skills and deterioration in adaptive self-care skills including bowel and bladder control, eating, dressing and undressing. Within several months, the boy reached a state of overtly bizarre behavior and dementia and was saying nothing. At the clinic, the boy showed marked repetitive movements and was rather uncontrollable and tried to move from place to place in the room.



Figure 2M: A four-year old boy with Heller syndrome. He who was considered normal until shortly after the age of two and half years when the family thought that he was gradually becoming stupid with gradual deterioration of social interaction. Thereafter, he experienced loss of adaptive self-care skills with loss of bowel control and the development of repetitive behaviors. At the clinic, the boy was not saying any word, but he was responding to his name and had some eye contact, but he was not communicating or responding to any question or request. He showed marked repetitive behaviors.

In the first nineteen patients observed initially during the period from December, 2017 to January, 2019 [10]. Only eight patients (Seven males and one female) were treated with the new therapeutic approach. The patients' ages ranged from 3 to 8 years. Seven patients had a diagnosis of autism and one

patient had a diagnosis of Asperger syndrome (Patient 5). Risperidone was used in one patient.



Figure 3A: One of the patients with typical autism was boy who had spastic cerebral palsy and was having difficulties in standing and walking.



Figure 3B: A girl with atypical autism associated with severe mental retardation and her condition was secondary to phenylketonuria. She was very irritable and was very difficult to control at the clinic.



Figure 3C: An eight-year-old boy with severe atypical autism

associated with significant behavioral abnormalities including biting his sister; at the clinic he displayed significant repetitive movements.



Figure 3D: A seven-year old boy with classic autism (Kanner syndrome). He had impaired social interaction and communication dominated by the lack of response to his name and poor eye contact.

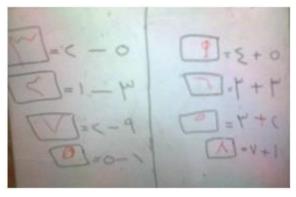


Figure 3E: A seven-year old boy with classic autism (Kanner syndrome) who had impaired social interaction and communication dominated by the lack of response to his name and poor eye contact. However, the mother demonstrated that he has no cognitive impairment as he write could words and solve simple math problems. Table 1 shows the courses of therapy received by the eight treated patients in the first 19 patients [10] observed during the period from December, 2017 to January, 2019).

The second group of patients observed initially during the period from 18, November, 2018 to 18, July, 2019 included 51 patients.

Thirty-two (17 males and 15 females) patients had

autism without significant mental retardation as indicated by adequate urine and bowel control and self-care skills particularly spoon feeding. They were considered to have typical autism.



Figure 4A: Figure shows the second patient after treatment. After completion of four courses of treatment (Table 1), the boy social interaction was perfectly normal with acceptable looking at face and eye contact. He was normally responding to calling his name.



Figure 4B: Patient 3 after treatment (Table 1). The boy showed normal social interaction manifested by appropriate response to his name, normal eye contact, responding to the doctor when asked him to take the pen and tried to draw a line and a circle. He also waved goodbye when leaving the examination room.



Figure 4C: Figure shows patient 4 after treatment (Table 1). At the clinic, the boy social interaction was perfectly normal with acceptable looking at face and eye contact. He was normally responding to calling his name, talking with doctor.



Figure 4D: Patient 6 after the third course of treatment (Table 1). She had good eye contact and was responding to her name. She accepted to take a pen to copy a line. She tried to copy a line, a circular figure and then she started scribbling. She also accepted to take a photo with the doctor.



Figure 4E: Patient 8 after the six months of treatment (Table 1). He

had normal social interaction with good eye contact and was responding to his name. He accepted to take a photo with the doctor.



Figure 5: The sixteen-year-old boy who received before referral many therapeutic interventions and special education, but continued to have severe autistic features and was unable to say any word.



Figure 6A: At the clinic, after treatment, the boy was more controllable and showed much less body rocking movements. The parents was convinced that he was not deaf.



Figure 6B: The girl with Asperger syndrome. At the clinic, after 10 days of treatment, her behavior and emotional swinging improved.



Figure 6C: The six-year-old boy with typical autism in Figure 2A after treatment (Table 2). At the clinic, the boy had normal social interaction with appropriate response to his name. He was greeting the doctor and waving goodbye when leaving the clinic.



Figure 6D: Figure shows the seven-year old girl with typical autism in Figure 3B after treatment. The girl had normal social interaction and she responded to the doctor request to take a pen and copy something.



Figure 6E: The seven-year old girl with typical autism in Figure 3B after treatment. She also waved goodbye when she was leaving the clinic in response to the doctor waving goodbye.

Figure 2A shows a six-year-old boy with typical autism before treatment. He had impaired social interaction as he was not responding appropriately to calling his name was showing no eye contact. The boy was treated for six months during which, he received 60 doses of

Intramuscular cerebrolysin 5 ml every third day in the morning. He also received trifluoperazine 1 mg at night and prochloperazine 5 mg during the afternoon during the early months of treatment. He also received oral citicoline 2 to 3 (200 mg to 300 mg) ml in the morning daily few months.



Figure 6F: The seven-year old girl with typical autism who was totally not responsive before treatment. After treatment, the girl had normal social interaction and she responded to the doctor request to take a pen and copy something. She also accepted taking a photo with doctor.



Figure 6G: A girl with autism who joined private school after six

months treatment was her teachers reported that was the most intelligent pupil in her class. At the clinic she had normal social interaction and accepted to take a photo with the doctor.



Figure 6H: One of the boys with Asperger syndrome after four months of treatment. At the clinic, the boy had normal social interaction with appropriate response to his name. He was greeting the doctor and waving goodbye when leaving the clinic.



Figure 7: The second patient in the third group who experienced complete disappearance of the main autistic features: After treatment, they had acceptable social interaction and communication. He accepted the doctor request to take a pen to write something without the need for the help of mother and he easily accepted to take photo with the doctor. He also waved goodbye in response to the doctor. Figure 2B shows a seven-year old girl with typical autism before, she had impaired social interaction as she was not responding appropriately to her name was showing no eye contact. She also showed frequent repetitive movements. Table-2 shows the courses of treatment the girl received.

Four boys were considered to have a severe form of the disorder, one of them, the parents thought the child was

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deaf and consulted initially an ear specialist. One boy had prominent echolalia.

Table 1 (Cont.): The courses of therapy received by the eight treated patients in the first 19 patients observed during the period from December, 2017 to January, 2019).

	Age (year	Sex	Treatment
Patient 1	Four Mal		Ten intramuscular injections of cerebrolysin, four ml given every third day over
(Figure 1A)	1 Out	e	one months.
			The first course consisted of ten intramuscular injections of cerebrolysin, 1 ml
		Mal e	given every third day over one month.
			The second course:
	Three		A-Six intramuscular injections of cerebrolysin, 1 ml given every five days over one month.
Patient 2			B-Six intramuscular injections of citicoline, 2 ml given every five days over one
(Figure 1B)			month.
, 0			The third course:
			A-Ten intramuscular injections of cerebrolysin, 3 ml given every three days over one month.
			B-Citicoline syrup, 3 ml orally daily as a single dose in the morning.
			The fourth course of therapy consisted of ten intramuscular injections of
			cerebrolysin, four ml given every 3 days over one month.
			The first course:
			A-Ten daily injection of cerebrolysin, 1 ml intramuscularly over ten days.
			B-Oral trifluoperazine 1 mg at night.
Patient 3	Three	Mal	The second course:
(Figure 1C)	Three	e	A-Ten daily injection of cerebrolysin, 3 ml every third intramuscularly.
			Over one month.
			B-Oral trifluoperazine 1 mg at night.
			C-Citicoline syrup, 3 ml orally daily as a single dose.
Patient 4	Five	Mal	A-Ten daily injection of cerebrolysin, 3 ml intramuscularly over ten days.
(Figure 1D)	½	e	B-Oral trifluoperazine 1 mg at night.
Patient 5 (Figure 1E)	Eight	Mal e	Ten doses of 1 ml cerebrolysin by intramuscular injection every other day.
	Six	Fe mal e	The first course:
Patient 6			A-Ten daily injection of cerebrolysin, 3 ml every third day intramuscularly over one month.
			B-Oral trifluoperazine 1 mg at night.
			C-Prochloperazine 5 mg tablet daily taken during the afternoon.
			The second course of:
			A-Ten daily injection of cerebrolysin, 5 ml every third day intramuscularly over one month.
			B-Oral trifluoperazine 1 mg at night.
			C-Prochloperazine, 5 mg tablet daily taking during the afternoon.
			D-Risperidone 0.5 mg daily at night during the first week thereafter continued at
			1 mg dose daily.
			The third course of treatment was the same as the third course, but with addition
			of Citicoline (Somazina) syrup, 3 ml orally daily as a single dose.
Patient 7	Six	Mal e	Three courses of treatment over three months and included:
			A-Intramuscular cerebrolysin 5 ml every third day given over one month.
			B-Trifluoperazine in a daily dose of 5 mg at night

			C-Prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month.		
Patient 8	Six	Mal e	Six courses of treatment over six months included:		
			Trifluoperazine in a daily dose of 5 mg at night		
			Prochloperazine in a daily dose of 5 mg in the afternoon.		
			Intramuscular cerebrolysin 5 ml every third day given over one month.		

Table 2: The courses of treatment received by a seven-year-old girl (Figure 3B) who experienced complete disappearance of the autistic features.

First treatment course given during February, 2019.				
Intramuscular cerebrolysin 5 ml every third day.				
Trifluoperazine in a daily dose of 1 mg in the morning.				
Second course started on the fourth of March, 2019				
Intramuscular cerebrolysin 5 ml every other day.				
Trifluoperazine in a daily dose of 1 mg in the morning.				
Oral citicoline 3 ml (300 mg) in the morning.				
Third course started on the 18 th of April, 2019.				
Intramuscular cerebrolysin 5 ml every third day, 10 doses.				
Prochloperazine in a daily dose of 2.5 mg at night.				
Oral citicoline 3 ml (300 mg) in the morning.				

Table 3: Courses of treatment received by a boy in the second group who was thought to be deaf by parents (Figure 3D).

First treatment course started on the 17th of January 2019.

A-Intramuscular cerebrolysin 5 ml every other day, 10 doses.

B-Oral trifluoperazine in a daily dose of 5 mg at night

C-Oral prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month.

Second and third courses of treatment

A-Intramuscular cerebrolysin 5 ml every other day, 10 doses monthly.

B-Oral trifluoperazine in a daily dose of 1 mg in the moring.

C-Oral prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month.

D-Oral risperidone 1 mg at night.

The seven courses received over seven months

A-Intramuscular cerebrolysin 5 ml every other day, 10 doses monthly.

B-Oral trifluoperazine in a daily dose of 1 mg in the moring.

B-Oral trifluoperazine in a daily dose of 1 mg in the moring.

C-Oral prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month.

D-Oral risperidone 2 mg at night.

E- Oral citicoline 3 ml (300 mg) in the morning.

Table 4: Courses of treatment received by the boy with severe autism associated with mental retardation who was overweight (Figure 8H).

First treatment course started on the 17th of January 2019 A-Intramuscular cerebrolysin 5 ml every other day, 10 doses. B-Oral trifluoperazine in a daily dose of 5 mg at night. C-Oral prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month. Second and third courses of treatment A-Intramuscular cerebrolysin 5 ml every other day, 10 doses monthly.

C-Oral prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month.

D-Oral risperidone 1 mg at night.

The seven courses received over seven months

A-Intramuscular cerebrolysin 5 ml every other day, 10 doses monthly.

B-Oral trifluoperazine in a daily dose of 1 mg in the moring.

C-Oral prochloperazine in a daily dose of 5 mg in the afternoon was added during the third month.

D-Oral risperidone 2 mg at night.

E- Oral citicoline 3 ml (300 mg) in the morning.

Table 5: Courses of treatment received by the boy in Figure 3D.

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FIRST COURSE						
1-Intramuscular cerebrolysin 5 ml every other day (10 doses)						
2-Trifluoperazine 1 mg in the morning						
3-Prochloperazine 2.5 mg in the afternoon						
SECOND COURSE						
1-Intramuscular cerebrolysin 5 ml every third day (10 doses over 30 days)						
2-Trifluoperazine 1 mg in the morning						
3-Prochloperazine 5 mg in the afternoon						
4-Oral citicoline 3 ml (275 mg) in the morning						

Figure 2C shows an eight-year old boy with severe autism and had significant behavioral abnormalities. He was not saying any word. At the clinic, he was unable to sit still on the chair without frequently changing the position of his body. He also displayed marked repetitive behavior at the clinic. Figure 2D shows a three-year boy with severe autism which made his parents thought him to be deaf, but hearing assessment showed that the boy had normal hearing. At the clinic the boy was rather uncontrollable and displayed marked repetitive movements in the form of body rocking and was trying to leave the room. The boy in Figure 2D received three courses of treatment (Table-3).

The patients in this group didn't have significant mental retardation and were classified as having rather typical autism, but most of them had developmental delay particularly in fine motor skills and had some cognitive impairment manifested by their inability to copy forms.

However, the serious lack of communication skills per she is expected to prevent or delay the acquisition of such developmental mile stones. Figure 2E and Figure 2F show an eight-year boy and a six-year boy with autism who were unable to copy a circle.

In the second group of patients, thirteen patients were considered to have atypical autism or pervasive developmental disorder not otherwise specified (10 boys and 3 girls), in eleven of them, the disorder was considered atypical because of the association with significant degree of mental retardation as indicated by the lack of adequate adaptive skills particularly urine and bowel control and lack of self-care skills especially appropriate spoon feeding.

One patient was considered to have atypical autism because of the presence of an acceptable eye contact and response appropriately to name in most instances. Six patients (five boys and one girl) were considered to have a severe form of the disorder. At the clinic, one of the boys with severe disorder was behaving as if he was absolutely not seeing or hearing the doctor for more than five minutes.

A five-year old girl was considered to have the mildest disorder among patients with typical and a typical autism (Figure 2G). Although she didn't have eye contact and was not responding to calling her time, she was sometime answering questions like how are you and was responding to request of the doctor with the encouragement of her parents.

One boy with severe condition was overweight (Figure 2H) and the mother thought that his sister had the same condition, but she couldn't brought her for consultation because the parents were divorced and the girl was under the care of her father. At the clinic the boy was uncontrollably hyperactive and showed marked repetitive movements. The treatment of the boy with severe autism associated with mental retardation who was overweight (Figure 2H) is summarized in Table 4. He received 10 courses of treatment over 10 months.

Another boy with atypical autism had infantile left hemiplegia and seizures and another boy had small ventricular defect during infancy. One boy with atypical autism developed insulin dependent diabetes mellitus.

A four and half years old girl had brain arachnoid cyst on CT scan and MRI. Brain CT-scan at the age of four years showed right anterior basal temporal small arachnoid cyst (23 X 7 X 16 mm). CT-scan also showed that the cisterna points and C-P cisterns were prominent on both sides with low density. The CT-scan report also suggested the possibility of epidermoid cyst. Brain MRI confirmed the presence of a right anterior basal temporal (24 X 8 X 17 mm) with clean CSF. MRI also showed atrophic changes of the right temporal lobe.

Figure 2I shows the eight-year old girl with atypical autism which was considered to have the most severe disorder among the patients with typical and atypical autism. She was totally uncontrollable and irritable.

In the second group of patients, three patients had Asperger syndrome including two girls and one boy. A seven-year old girl with Asperger syndrome was considered to have the mildest form among all the patients (Figure 2J) in this series, with good language

development and response to many requests with the encouragement of the mother. She also welcomed taking a photo with doctor. However, her social interaction was impaired as she was not responding appropriately to her name and was not showing acceptable eye contact.

A nine years old girl with Asperger syndrome and good language development, but she had delayed onset of speech after four years. We think that this patient represents a variant of Asperger syndrome with late onset development of language can initially misdiagnosed as a case of autism.

Her measured IQ test ranged from 85 to 110. She left school because of poor social interaction and communication and emotional fluctuation. At the clinic, she showed alternating mood, she was smiling and almost crying with in the same minute and without obvious reason (Figure 2K). Initial treatment of this patient included:

Intramuscular cerebrolysin 5 ml daily for 10 days.

Oral trifluoperazine in a daily dose of 1 mg at night.

Oral prochloperazine 5 mg in the afternoon.

In the second group of patients, two boys (Figure 2M and 2L) had childhood disintegrative disorder (Heller syndrome), one of them have changes on brain MRI suggestive of cerebral vasculitis. The case of the two boys was previously reported [9].

The second group of patients also included three-year girl had Rett syndrome and her case and early treatment was published [7]. She was hypotonic, ataxic and had abnormal movements of the upper limbs. She was unable to sit alone on a chair and showed no eye contact and was not responding to her name. She didn't have purposeful hand movement and was not able to hold things. She couldn't be held erect in the standing position. She was not saying any word nor was babbling. The girl received two treatment courses. The first course included intramuscular cerebrolysin 1ml daily for ten days. The second course included 10 cerebrolysin injections, 3ml every third day and oral citicoline.

The third group of patients was observed during the period from June, 2019 to November, 2019.

It included forty-six new patients (38 males and eight females). Twenty-four patients (52%) including 20 boys and 4 girls received a diagnosis of typical autism based on the lack of obvious evidence of mental retardation and acceptable adaptive behaviors including bowel control and good spoon feeding.

Four of the 21 patients with typical autism including three boys and one girl were considered to have classic autism (Kanner syndrome) as it was possible to demonstrate that they had good intelligence.

Two male patients in this group had significant echolalia including one of the patients with classic autism (Kanner syndrome) and one boy with classic autism (Kanner syndrome) had Occasional echolalia. One boy had significant aggressive behavior and was frequently beating his mother.

One boy had spastic cerebral palsy and was having difficulties in standing and walking (Figure 3A). A girl in this group had brain MRI which showed normal findings and a boy with classic autism (Kanner syndrome) had brain CT-scan which also showed normal findings.

In the third group of patients, seventeen patients (37%) including 14 boys and 3 girls received a diagnosis of atypical autism based on evidence of mental retardation indicated by poor and late development of adaptive behaviors including bowel control and good spoon feeding.

In one girl, atypical autism was secondary to phenylketonuria (Figure 3B). Four patients were brothers each two of them from two unrelated families. Significant behavioral abnormalities including biting others including sibling was observed in three boys, one of them also had gait abnormalities attributed to birth asphyxia and his CT-scan showed evidence of slight brain atrophy with mild dilatation of the ventricular system. Figure 3C shows an eight-year-old boy with severe atypical autism associated with significant behavioral abnormalities including biting

his sister; at the clinic he displayed significant repetitive movements.

Figure 3D shows a seven-year old boy with classic autism (Kanner syndrome) who had impaired social interaction and communication dominated by the lack of response to his name and poor eye contact. However, the mother demonstrated that he has no cognitive impairment as he write could words and solve simple math problems (Figure 3E). Table-5 shows the two courses of treatment received by the boy in Figure 3D over 50 days.

Four patients including three boys and one girl (8.7%) received the diagnosis of Asperger syndrome with acceptable language development by definition.

One boy was considered to have pervasive developmental disorder otherwise not specified because despite impaired social interaction and communication dominated his disorder, he lacked the typical features of poor eye contact and non-response to his name.

In the third group of patients, twenty six (66.6%) patients received neuroleptic to control significant over activity and other behavioral abnormalities; six of them required triple neuroleptics therapy (Trifluoperazine, prochloperazine, risperidone), thirteen patients received two neuroleptics (Trifluoperazine and prochloperazine), five patients received only trifluoperazine approchloperazine and two patients received only prochloperazine). Three patients received oral citicoline during the follow-up period with the aim of initiation or improving speech.

5. Results

In the first nineteen patients (observed during the period from December, 2017 to January, 2019), all the seven patients with autism and the patient with Asperger syndrome treated with the new therapeutic approach experienced improvement and marked lessening of the autistic features with six patients (Patients 1-4,6,8 (Table 1)) showed complete disappearance of the main autistic features. The fifth patient with Asperger syndrome received a short course with relatively very

small dose compared to other patients. Treatment was also associated with initiation of speech and improvement of repetitive behaviors. When these six patients were examined by physicians after treatment, the physicians couldn't identify any autistic feature and didn't make the diagnosis of an autistic disorder or autism. No patient developed any side effects. It seems that the six patients who achieved complete disappearance of the main autistic features will need an intensive learning especially of speech to abolish the effect of the time when they were under the effect of autistic behavior and to push them toward a possible cure of their illness. Figure 4A shows the second patient after treatment. After completion of four courses of treatment (Table 1), the boy social interaction was perfectly normal with acceptable looking at face and eye contact. He was normally responding to calling his name. The boy was happy when the doctor asked him to take a photo together. The parents reported obvious improvement in his speech. Figure 4B shows patient 3 after treatment (Table 1). The boy showed normal social interaction manifested by appropriate response to his name, normal eye contact, responding to the doctor when asked him to take the pen and tried to draw a line and a circle. He also waved goodbye when leaving the examination room.

Figure 4C shows patient 4 after treatment (Table 1). At the clinic, the boy social interaction was perfectly normal with acceptable looking at face and eye contact. He was normally responding to calling his name, talking with doctor. His mother reported lessening of hyperactivity and improvement of his responsiveness and speech. Figure 4D shows patient-6 after the third course of treatment (Table 1). She started babbling and was having good eye contact and was responding to her name. She accepted to take a pen to copy a line. She tried to copy a line, a circular figure and then she started scribbling. She also accepted to take a photo with the doctor. Figure 4E shows patient 8 after the six months of treatment

(Table 1). He had normal social interaction with good eye contact and was responding to his name. He also accepted to take a photo with the doctor. The boy was able to study at private primary school as governmental schools don't accept joining primary school at his age. Ten of eleven patients observed during the same year who didn't receive this treatment or were treated with other treatments such as omega-3 and risperidone didn't show any lessening effect in the autistic features. A striking example of these patients was a sixteen years old boy who received before referral many therapeutic interventions and special education, but continued to have severe autistic features and was unable to say any word (Figure 5).

In the second group of patients observed initially during the period from 18, November, 2018 to 18, July, 2019. It was not possible to document the treatment details of all patients. However, most patients experienced some improvement during follow-up including one of the boys with Heller syndrome (Figure 2M) and the girl with Rett syndrome. The boy in the second group of patients who was thought to be deaf by the parents (Figure 2D), after three courses of treatment (Table 3), the improvement was enough to convince the parents that the child was not deaf. At the clinic, after treatment, the child was more controllable and showed much less body rocking movements (Figure 6A). Treatment was also associated with initiation of speech and improvement of repetitive behaviors in many patients.

The nine years old girl with Asperger syndrome (Figure 2K) and good language development, After 10 days of treatment, her behavior and emotional swinging improved. She became rather passionate and when leaving she insisted on hugging the doctor and kissing him (Figure 6B).

It was possible to document complete disappearance of the main autistic features (Impaired social interaction and communication dominated by the lack of response to their name and poor eye contact) in 10 patients including the six year old boy with typical autism in Figure 3A, the seven-year old girl with typical autism in Figure 3B and two boys with Asperger syndrome. Figure 6C shows the six-year-old boy with typical autism in Figure 2A after treatment. At the clinic, the boy had normal social interaction with appropriate response to his name. He was greeting the doctor and waving goodbye when leaving the clinic.

Figure 6D shows the seven-year old girl with typical autism in Figure 2B after treatment. The girl had normal social interaction and she responded to the doctor request to take a pen and copy something. She also waved goodbye when she was leaving the clinic in response to the doctor waving goodbye (Figure 6E). Figure 6F shows the seven-year old girl with typical autism who was totally not responsive before treatment. After treatment, the girl had normal social interaction and she responded to the doctor request to take a pen and copy something. She also accepted taking a photo with doctor.

Figure 6G shows a girl with autism who joined private school after six months of treatment was her teachers reported that was the most intelligent pupil in her class. At the clinic she had normal social interaction and accepted to take a photo with the doctor.

Figure 6H shows one of the boys with Asperger syndrome after four months of treatment. At the clinic, the boy had normal social interaction with appropriate response to his name. He was greeting the doctor and waving goodbye when leaving the clinic.

The boy with severe autism associated with mental retardation who was overweight (Figure 2H) showed complete disappearance of the main autistic features after ten courses of treatment (Table 4). He was responding to name and had good eye contact, but he remained obviously mentally retarded having poor cognition and poor adaptive behaviors and his speech was not developed.

In the he third group of patients which was observed during the period from June, 2019 to November, 2019.

All the patients experienced some improvement during

follow-up. It was possible to document complete disappearance of the main autistic features (Impaired social interaction and communication dominated by the lack of response to their name and poor eye contact) in four patients.

The first patient was a five-year old boy with typical autism, who was first seen during June, 2019. He had poor language development and impaired social interaction and communication dominated by the lack of response to his name and poor eye contact. He received three courses of intramuscular cerebrolysin over three months period. In the first course, he received cerebrolysin 3 ml every other day (10 doses). In the second course, he received cerebrolysin 5 ml every other day (10 doses). In the third course, he received cerebrolysin 5 ml every other third (10 doses). During the three courses, he was also receiving trifluoperazine 1 mg at night.

Treatment was started on 20th of June, 2019, when the boy was seen after completing the three treatment courses on the 19th of September, he didn't have the main autistic features as he responding to name, greeting and talking with doctor with good eye contact and with obvious improvement in his speech.

The second patient was a seven-year old boy with classic autism (Kanner syndrome) who was first seen during August, 2019 (Figure 3D, treatment in Table 5). He had poor language development and impaired social interaction and communication dominated by the lack of response to his name and poor eye contact. He had prominent repetitive movements also. He had very good adaptive skills and the mother demonstrated that he has no cognitive impairment as he write could words and solve simple math problems.

After treatment, the boy had acceptable social interaction and communication with improved speech. He was normally responding to his name and had good eye contact. He accepted the doctor request to take a pen to write something without the need for the help of mother and he easily accepted to take photo with the doctor. He also waved goodbye in response to the

doctor (Figure 7).

In addition to these two boys, another two boys, one with atypical autism and one with atypical autism also experience complete disappearance of their main autistic features.

6. Discussion

Impairment of social interactions is the most important distinguishing feature that makes autism and other autistic disorders distinctive from other developmental disorders. Marked improvement or disappearance of autistic features in these disorders has not been reported with any therapy before [1,5,10,11].

Cerebrolysin is a mixture of free amino acids (85%) and 15% biologically active low molecular weight amino acid sequences which include low molecular weight neuro-peptides (Brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, nerve growth factor, ciliary neurotrophic factor [12]. Cerebrolysin has been used safely with benefit in a variety of neuro-psychiatric disorders including idiopathic mental retardation [13-16], cerebral palsy [17-19], brain atrophy [20], myelomeningocele [21], pediatric juvenile spinal muscular atrophy [22,23], pediatric Charcot Marie Tooth disease [24,25], kernicterus [26-28], agenesis of corpus callosum with colpocephaly [29,30].

Citicoline (cytidine diphosphate-choline) or cytidine 5 diphosphocholine is a psycho-stimulant/nootropic. Citicoline has a very low toxicity and has been approved for treatment of head trauma, stroke and neurodegenerative disease in Japan and Europe [31,32].

7. Conclusion

In this paper, we have demonstrated the possibility of cure of autistic disorders including autism and Asperger syndrome with use of individualized courses of intramuscular cerebrolysin as the main therapy for the main autistic features (Impaired social interaction and communication dominated by the lack of response to their name and poor eye contact).

Understanding, a cure of autism will not immediately

abolish the cumulative effect of the condition on learning, behavior and speech development before cure.

8. Acknowledgement

1-The author would to express his gratitude for the parents of the patients who accepted publishing their photos.

2-Many figures were previously published and the author has their copyright.

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Citation: Aumir Jalai Al-Mosawi. Cure of autistic disorders: Mission impossible is possible in an illustrated pioneering experience. SunKrist J				
Psychiatry Ment Health 2020: 1: 1003	sorders: Mission impossible	is possible in an illustrate	d pioneering experience. S	SunKrist J
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