



Mesenchymal Stem Cell Infusion is Consistently Effective in Improving Autism Behavioral Parameters and EEG Metrics

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Introduction

Autism Spectrum Disorder (ASD) is a neuro-developmental disorder that has shown a steady recent escalation in occurrence. ASD has increased from 1 in every 150 children in 2000 to 1 in every 50 children in 2020 [1]. Numerous studies have shown autism to be immune-mediated (REF), which has brought forth the possibility of treating ASD with Mesenchymal Stem Cells (MSCs) which are immunomodulatory [2]. For example, significantly elevated levels of C-Reactive Protein (CRP),

a protein released by the liver in response to systemic inflammation, are observed in children with ASD when compared to healthy controls [3,4]. MSCs have been shown to treat other immune-mediated or autoimmune disorders. These disorders include but are not limited to Inflammatory Arthritis, Inflammatory Bowel Disease, Multiple Sclerosis, Autism, and Graft-Versus-Host Disease [5-18]. An Electroencephalogram (EEG) is a test that measures the brain's electrical activity and can be

Abstract

Background: Autism Spectrum Disorder (ASD) produces troubling behavior and affected one in every thirty-six children in 2020. There is no cure and no reliable treatment. Intravenous Mesenchymal stem cell (MSC) infusion has provided efficacy in limited prior studies.

Methods: Inclusion criteria were diagnosis of ASD by an appropriate medical specialist and minimum six-month follow-up after MSC treatment. Evaluation included Autism Spectrum Rating Scale (ASRS) pre and post treatment. And a global improvement assessment post treatment. Electroencephalogram (EEG) was performed pre and post treatment in three patients.

Results: Eight patients met criteria. All had significant improvement one month after treatment. Seven of the eight patients had significant improvement minimum six months post treatment by both Global Improvement and ASRS ratings. The three EEG evaluated patients all showed significant improvement post treatment. No minor or severe adverse events occurred in any patient. One patient had longstanding absence seizures which almost completely disappeared for the full two years of his latest follow-up.

Conclusions: MSC IV infusion was shown to be consistently, significantly effective reducing symptoms in a high (88%) percentage of ASD patients with results extending minimum six months post treatment, and usually much longer, with no adverse events seen.



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used to detect abnormalities. A component that an EEG can measure is the functioning of the autonomic nervous system. The autonomic nervous system comprises two major systems: The sympathetic nervous system, commonly called the “fight or flight” system, and the parasympathetic nervous system, commonly called the “rest and digest” system. The sympathetic nervous system is typically associated with Beta brain waves and the parasympathetic nervous system is correlated with Theta brain waves. Patients with ASD have been shown to have higher sympathetic activity and lower parasympathetic activity.

We hypothesized that intravenous infusion of mesenchymal stem cells would significantly improve the clinical symptoms of autism patients and decrease their sympathetic brain wave activity while increasing their parasympathetic brain wave activity as measured by EEG.

Materials and Methods

Inclusion criteria for our study was clearly diagnosed, on clinical grounds, autism spectrum disorder. Patients had to have family members capable of providing proper informed consent. Minimum age was four, there was no maximum age.

Patients were evaluated using the Autism Scale Rating Scale (ASRS) short form as judged before and then after most recent treatment. Family members also gave a global assessment rating of the patient’s overall improvement. Patients who did not require sedation, and who were cooperative, were also evaluated with EEGs immediately before and then 2-3 months after treatment. Three patients met these criteria.

Three areas of the brain were measured. These areas were the Cerebral Cortex (Cz), Left Temporal Lobe (T3), and Right Temporal Lobe (T4). Cz is associated with essential brain functions such as learning and memory, while T3 and T4 are responsible for interpreting sounds and using one’s senses to understand and respond to the world. For every brain area, the EEG measured the High Beta (HB) and Theta (T) activity before and after treatments for comparison.

Results

Each patient who had an EEG had three brain areas measured, giving us a total of nine areas. Eight of these nine areas showed a significant increase in Theta wave activity after treatment. Our findings suggest that the stem cell treatment resulted in an increase in parasympathetic activity which lasted for at least 3 months following the stem cell intervention. Additionally, all three patients had a clinical reduction in their autism symptoms. This was seen in both the ASRS form and self-reported patient outcomes.

Ratings results

All patients showed improvement at 6 months except 1 patient who had improvement at 1 month but not thereafter. This is reflected in their improvement in both the ASRS form and self-reported symptoms. Out of a possible 60 points, there was a mean ASRS improvement of 10.5.

Global improvement

All patients had improvement and all parents thought the improvement was clinically significant. There was a mean global improvement of 32%.

Table 1: Patient Demographics and EEG Results.

DOB	Sex	Age (years)	Weight (kg)	MSCs treated with (millions)	MSCs/kg
12/22/1994	Male	29	84.82	150	1.77
10/16/2014	Male	9	31.75	100	3.15
11/25/1997	Male	26	75.75	150	1.98
12/1/1996	Female	27	113.39	200	1.76
12/4/2017	Male	6	18.14	50	2.76
7/11/2016	Male	7	33.57	60	1.79
11/5/2008	Female	15	65.77	125	1.90
3/30/2016	Male	7	20.59	100	4.86

Table 2: Timeline for EEG Recordings.

DOB	Sex	Pre-Treatment EEG Date	Treatment Date	Post-Treatment EEG Date
11/25/1997	Male	3/22/2022	4/2/2022	5/16/2022
7/11/2016	Male	9/9/2022	9/10/2022	11/25/2022
11/5/2008	Female	12/02/2022	12/02/2022	03/22/2023

Table 3: Change in Theta and High Beta Activity after Treatment.

DOB	Sex	Age (years)	Change in Electrode Activity					
			CZ Theta	CZ HB	T3 Theta	T3 HB	T4 Theta	T4 HB
11/25/1997	Male	24	2.0	-0.5	0.84	-0.53	0.78	-0.53
7/11/2016	Male	6	0.52	0.08	0.64	0.12	-0.27	0.92
11/5/2008	Female	14	1.69	-1.10	0.58	-1.71	0.99	0.21

Table 4: Theta Wave Measures Before and After Treatment.

DOB	CZ Theta Pre	CZ Theta Post	T3 Theta Pre	T3 Theta Post	T4 Theta Pre	T4 Theta Post
11/25/1997	2.32	4.32	1.89	2.73	1.52	2.3
07/11/2016	3.8	4.32	2.45	3.09	2.71	2.44
11/05/2008	2.33	4.02	1.64	2.22	2.15	3.14

Table 5: High Beta Wave Measures Before and After Treatment.

DOB	CZ HB Pre	CZ HB Post	T3 HB Pre	T3 HB Post	T4 HB Pre	T4 HB Post
11/25/1997	1.82	1.32	2.49	1.96	2.59	2.06
07/11/2016	1.37	1.45	1.73	1.85	1.6	2.52
11/05/2008	2.2	1.1	3.48	1.77	1.78	1.99

As seen above, 8 of the 9 areas where theta waves were measured experienced an increase in the theta waves which is associated with increased parasympathetic drive.

DOB	Pre ASRS	Post ASRS	Global Improvement	Latest Follow-Up	Language	Sleep	Appetite	Focus	Further Comments
12/22/1994	55	50	10%	24 months	-	Improved	-	-	No more ticks or seizures since treatment
10/16/2014	-	-	0%	12 months	-	-	-	-	-
11/25/1997	43	36	30%	6 months	-	Improved	-	-	Switched from Risperidone to Rexulti*
12/1/1996	39	34	30%	18 months	Improved	Improved	-	-	Improvement in stimming
12/4/2017	46	29	35%	18 months	-	-	-	Improved	
7/11/2016	22	5	55%	6 months	Improved	-	-	-	Improved confidence, eye contact, overall activity
11/5/2008	41	22	35%	12 months	Improved	-	Improved	Improved	-
3/30/2016	39	25	60%	6 months	Improved	-	Improved	-	Improved coordination and reading ability

Other areas of improvement

These are shown in the table and included sleep, calmness, verbal skills, seizure activity and other parameters. 50% of the patients treated reported an improvement in language while 38% reported an improvement in sleeping. Further improvements are shown in the above table.

Satisfaction: All patients thought the treatment worthwhile. Most have already or are planning to repeat the treatment.

Discussion

While this is a small sample size the results are very promising. These findings support the need for future research on the effects of MSC on ASD. This is especially true because of the severe social and financial ramifications of ASD. Nearly half of 25-year-olds diagnosed with autism have never held a paying job. The cost of caring for Americans with autism was \$268 billion in 2015 and is projected to rise to \$461 billion by 2025 [19]. With increasing rates of autism, novel therapies should be considered and as we learn of the immunomodulatory properties of ASD, MSCs emerge as a strong candidate for treatment. Long-term changes in EEG activity as well as even longer changes in clinical symptoms are a significant advancement in the treatment of ASD. A strength of our study is that we had both clinical and medical imaging improvements as seen by the change in the EEGs and the increase in the sociability of patients. A limitation of our study is that our study had a small sample size of only 3 patients.

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