

# Autologous Bone Marrow Derived Intrathecal Stem Cell Transplant for Autistic Children - A Report of Four Cases and Literature Review[1]

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## Abstract

Despite steadily growing numbers of children diagnosed with autism spectrum disorders (ASD), causative treatment is unavailable. Recently, biological cell therapies involving pluripotent cells have raised hopes towards sustained beneficial outcome. We herein report data of four children diagnosed with ASD, who were treated with autologous, bone marrow (BM)-derived, intrathecally and simultaneously intravenously applied, point-of-care stem cell transplant (SCT). The three boys and one girl received the diagnosis at ages between 2-4 years. The decision to perform the procedure was preceded by limited beneficiary impact of conventional symptom-based, psychological and pharmacological interventions. At ages of 4-14 years the children received their SCT, no immediate or late adverse events were reported. Disappearance of symptoms were observed by the parents during the following year and consequently improved Autism Treatment Evaluation Checklist (ATEC) scores were reported. The SCT procedure, in trained hands, can be a safe and promising treatment option in children with ASD, responding in a non-satisfactory manner to conventional treatments. It is postulated that SCT may, among others, assert its positive effect by counteracting a cerebral inflammatory autoimmune process which in turn supports the responsiveness to behavioral and pharmacological interventions. Our results in this small group are encouraging, but certainly need further investigation in larger cohorts.

**Keywords:** autism; autologous; bone marrow (BM); case report; intrathecal; point-of-care method; safety; stem cell transplant (SCT).

## Weitere Studien / further Studies

**Table 1a** Studies reporting regarding autologous stem cell transplantation for autistic children

	Sharma et al. [2]	Lv et al. [3]	Dawson et al. [4]	Chez et al. [5]
Journal (year)	Stem Cells International 2013	J of Translational Med 2013	Stem Cells Translational Med 2017	Stem Cells Translational Med 2018
Study design	Open label proof-of-concept study	Controlled, non-randomized trial (Phase I/II)	Single-center phase I open-label trial	Placebo-controlled crossover study
Number of participants (gender, age)	32 (8f/24m; 3-33 years)	37 (1f/36m; 3-12 years)	25 (4f/21m; 2-6 years)	29 (4f/25m; 2-7 years)
Groups	32 BM	14 UCB 9 UCB+UC 14 controls (therapy)	25 UCB	14 UCB 15 placebo
SC isolation of	BM	UCB and UC	UCB	UCB
SC application	intrathecal	intravenous (4x)	intravenous (1x)	intravenous (1x)
Follow-up	26 months	4, 8, 16, 24 weeks	6 and 12 months	12 and 24 weeks
Safety	Procedure related minor AE 17.9% vomiting 10.7% nausea 7.1% pain at site of injection 7.1% pain at site of aspiration 3.6% spinal headache SCT-related major AE 6 transient increase in hyperactivity 3 seizures 1 persistent increase in hyperactivity till 6 months postSCT	3 minor AE (low grade fever) 0 major AE	9 related AE 5 allergic reaction 2 agitation 1 aggression 1 other psychiatric disorder 0 serious AE	3 ,probable' AE 2 renal/urinary disorders 1 constitutional symptom 14 'possible' AE 8 gastrointestinal disorders 4 renal/urinary disorders 2 constitutional symptom 0 serious AE
Efficacy	Sig. improvements from pre- to post-SCT of scores (ISAA, CGI, FIM, Wee-FIM)	Both groups (UCB und UCB+UC) showed sig. improvements (CGI, CARS, ABC) compared to controls	Sig. improvements from pre- to both post-SCT time points of scores (CGI, PDDBI, EOWPVT-4, EGT)	Trend (but not sig.) towards improvement of scores (EOWPVT-4, ROWPVT-4, SBFR/SBKN, ABC, CGI)

*Abbreviations:* ABC, Aberrant Behavior Checklist; AE, adverse event; BM, bone marrow; CARS, Childhood Autism Rating Scale; CGI, Clinical Global Impression scale; EGT, Eye Gaze Tracking of Social Stimuli; EOWPVT-4, Expressive One-Word Picture Vocabulary Test (4<sup>th</sup> edition); FIM, Functional Independence Measure; f, female; ISAA, Indian Scale for Assessment of Autism; m, male; PDDBI, Pervasive Developmental Disorder Behavior Inventory; ROWPVT-4, Receptive One Word Picture Vocabulary Test (4<sup>th</sup> edition); SBFR, Stanford Binet (5<sup>th</sup> edition) Fluid Reasoning; SBKN, Stanford Binet (5<sup>th</sup> edition) Knowledge subtests; sig, significant; SCT, stem cell transplantation; UC, umbilical cord; UCB, umbilical cord blood; VABS-3, Vineland Adaptive Behavior Scales (3<sup>rd</sup> edition).

**Table 1b** Studies reporting regarding autologous stem cell transplantation for autistic children

	Dawson et al. [6]	Sharifzadeh et al. [7]	Nguyen et al. [8]
Journal (year)	J Pediatr 2020	Asia Pac Psychiatry 2020	Stem Cells Transl Med 2021
Study design	2:1 randomized, placebo-controlled, double-blind study (Phase II)	parallel single-blinded randomized controlled trial	open-label uncontrolled clinical trial
Number of participants (gender, age)	180 (37f/143m; 2-7 years)	32 (5f/27m; 5-15 years)	30 (5f/25m; 3-7 years)
Groups	56 autologous UCB 63 allogeneic UCB 61 placebo	14 BM 18 controls	30 BM + behavioral intervention
SC isolation of	UCB	BM	BM
SC application	intravenous	intrathecal (2 times within 4 weeks) after culturing	intrathecal (2 times within 6 months)
Follow-up	6 and 12 months	6 and 12 months	6, 12 and 18 months
Safety	84 minor AE (29 placebo, 55 UCB) 16 infusion reactions (4 placebo, 12 UCB) 6 serious moderate AE (3 placebo!, 3 UCB)	no side effects	0 serious AE 70 minor AE (somehow related to intervention) -27 less associated (e.g. skin rash, fatigue,...) -17 may be related (e.g. mild fever, nausea, vomiting) -26 related (e.g. pain, venipuncture problems)
Efficacy	Trend for improvement in the allogeneic UCB group (CGI)	Sig. improvements regarding CGI-severity of illness	Sig. improvements regarding CARS and VABS

*Abbreviations:* ABC, Aberrant Behavior Checklist; AE, adverse event; BM, bone marrow; CARS, Childhood Autism Rating Scale; CGI, Clinical Global Impression scale; EGT, Eye Gaze Tracking of Social Stimuli; EOWPVT-4, Expressive One-Word Picture Vocabulary Test (4<sup>th</sup> edition); FIM, Functional Independence Measure; f, female; ISAA, Indian Scale for Assessment of Autism; m, male; PDDBI, Pervasive Developmental Disorder Behavior Inventory; ROWPVT-4, Receptive One Word Picture Vocabulary Test (4<sup>th</sup> edition); SBFR, Stanford Binet (5<sup>th</sup> edition) Fluid Reasoning; SBKN, Stanford Binet (5<sup>th</sup> edition) Knowledge subtests; sig, significant; SCT, stem cell transplantation; UC, umbilical cord; UCB, umbilical cord blood; VABS-3, Vineland Adaptive Behavior Scales (3<sup>rd</sup> edition).

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### ORTHOPÄDIE

Gelenksabnutzung-Arthrose  
Osteochondraler Defekt  
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Frakturheilung  
Lange Knochendefekte

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Rückenmarksverletzung  
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