



Azrieli National Centre for Autism
and Neurodevelopment Research

טיפול לאוטיזם?

פרופ' גל מאירי

היחידה הפסיכיאטרית לילדים ונוער
המרכז הרפואי והאוניברסיטאי סורוקה

המרכז הלאומי ע"ש עזריאלי לחקר אוטיזם ונורו-התפתחות
סורוקה ואוניברסיטת בן גוריון



Israel Ministry
of Science & Technology





1. הבסיס הביולוגי לאוטיזם לא ברור דיו – האם מדובר בהפרעה אחת? מספר הפרעות? איפה זה במוח?
2. אין כיום טיפול מרפא למאפייני הליבה
3. הטיפולים הקיימים כיום מפחיתים חלק מהסימפטומים הנלווים ומהתחלואה הנלווית
4. טיפולים ניסיוניים – נוסו ונבדקו רבים מאוד ומגוונים מאוד במהלך השנים, אך רובם לא נחקרו באופן מבוקר
5. אין מספיק מחקרים על טיפול ומחקרים רבים אינם מייצגים את הספקטרום כולו – עם דגש על ילדים ואנשים בתפקוד גבוה





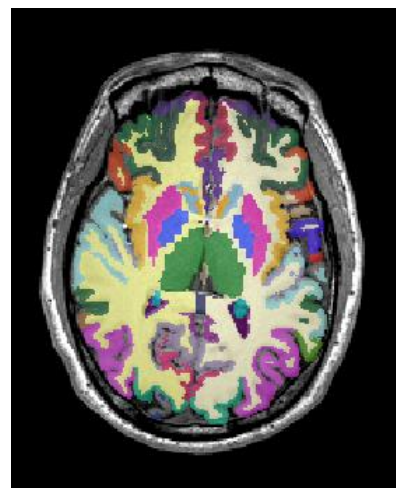
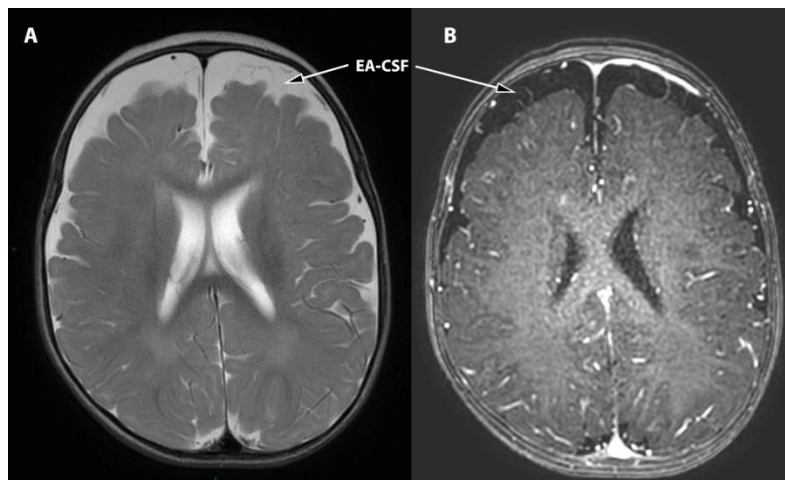


סימפטומים מגוונים – מה מטרת הטיפול?

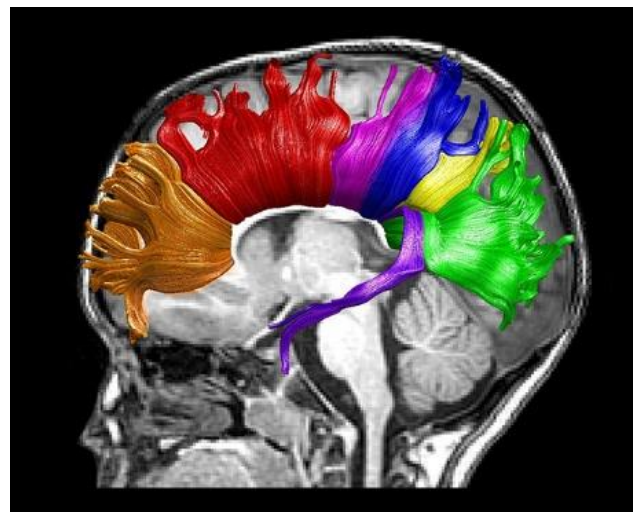
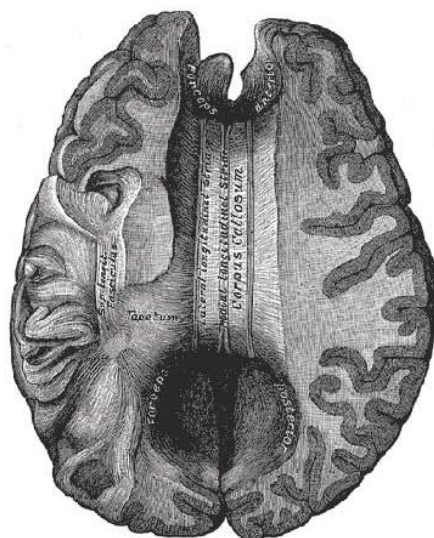




איפה זה במוח?? או מה עובד שונה?



- מבנה המח?
- תפקוד המח?
- קשרים בין אזורים במח?
- זרימת דם?
- אספקת חמצן?
- רצפטורים?
- נוירורנסמיטורים?



Dinstein et. al. Lancet Psychiatry 2019, Fingher et. al. Cortex, 2017



- Secretin Therapy
- Transdermal Secretin
- Nutritional Therapies and Autism
- Vitamin B-12
- Intramuscular or Intravenous Magnesium
- Gluten and Casein Free Diets
- Pancreatic Enzymes
- Omega-3 Fatty Acids
- Calcium
- Aloe Vera
- Flower of Sulphur
- Efalex Oil or DHA Oil
- Fibroblast Growth Factor 2
- Oral Organ Extracts
- Lyophilisate Whole Cells
- Anti-fungal Treatment
- Antibiotic Therapy to Improve Autism
- Naltrexone (NTX) Treatment
- IV Immunoglobulin Therapy
- Detoxification for Heavy Metals as a Treatment for Autism
- EEG Bio-feedback
- Traditional Chinese medicine
- Immunotherapy



1. טיפולים תרופתיים
2. קנאביס רפואי וצמחים אחרים
3. תאי גזע
4. אוקסיטוצין
5. תא לחץ - חמצן היפרברי
6. דיאטות שונות
7. מגנט TMS
8. סיכום





- טיפול תרופתי בילדים – האם מוצדק?
- טיפול תרופתי לילדים בספקטרום האוטיסטי – מה קורה בעולם?
- טיפול תרופתי לילדים בספקטרום האוטיסטי – האם לתת?
מתי ולמה?





תרופות פסיכיאטריות בילדים – מתי ולמה?



רציונל:

- בסיס ביולוגי להפרעות נוירו-פסיכיאטריות
- הפחתת סבל מהירה
- "זמן ילד"

נגד:

- לא ידועות השפעות לטווח ארוך
- "הרעלה בכימיקלים"
- שימוש כתחליף זול לפסיכותרפיה ולטיפולים אחרים.





J Autism Dev Disord (2017) 47:144–154
DOI 10.1007/s10803-016-2946-7

ORIGINAL PAPER

Psychotropic Medication Use among Insured Children with Autism Spectrum Disorder

Jeanne M. Madden^{1,2} · Matthew D. Lakoma² · Frances L. Lynch³ · Donna Rusinak^{2,8} ·
Ashli A. Owen-Smith^{4,5} · Karen J. Coleman⁶ · Virginia P. Quinn⁶ · Vincent M. Yau^{7,9} ·
Yinge X. Qian⁷ · Lisa A. Croen⁷



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Table 2 Prevalence psychotropic medication use and average months supplied by therapeutic class, for children with and without ASD in 2010

Therapeutic class	Percentage receiving any medication in class		Difference in likelihood of any use in year, ASD vs. no ASD		Average months supplied per user per year	
	Children with ASD (n=7901)	Children with no ASD (n=79,010)	Adjusted OR (95% CI)	p value	Children with ASD and any use	Children with no ASD and any use
All psychiatric medications	48.47	7.7	11.44 (10.02,13.06)	<0.0001	18.3	9.3
All ADHD medications	30.24	5.13	8.44 (7.61, 9.37)	<0.0001	12.3	9.9
Stimulants	22.73	4.76	6.12 (5.51, 6.81)	<0.0001	11.5	9.4
Other ADHD ^a	12.35	0.84	17.53 (15.42,19.93)	<0.0001	9.0	7.1
Antipsychotics	20.50	0.64	40.50 (35.25,46.53)	<0.0001	10.5	7.2
2nd generation	20.30	0.60	42.58 (36.99,49.01)	<0.0001	10.4	7.4
1st generation	0.39	0.04	9.55 (5.85,15.60)	<0.0001	7.3	2.3
Antidepressants	17.83	1.42	13.65 (11.88,15.69)	<0.0001	9.5	6.7
All mood stabilizers	9.07	0.55	17.20 (14.77, 20.02)	<0.0001	11.7	9.3
Anticonvulsants	8.72	0.53	17.07 (14.67,19.88)	<0.0001	11.5	9.1
Lithium	0.58	0.03	19.80 (12.24,32.02)	<0.0001	9.5	10.4
Benzodiazepines	4.30	0.48	8.96 (7.68,10.46)	<0.0001	2.8	1.6
Anti-anxiety medications	3.00	1.16	2.62 (2.22, 3.10)	<0.0001	3.3	1.1
Hypnotics	0.20	0.02	(nonconvergent)	–	2.9	1.6

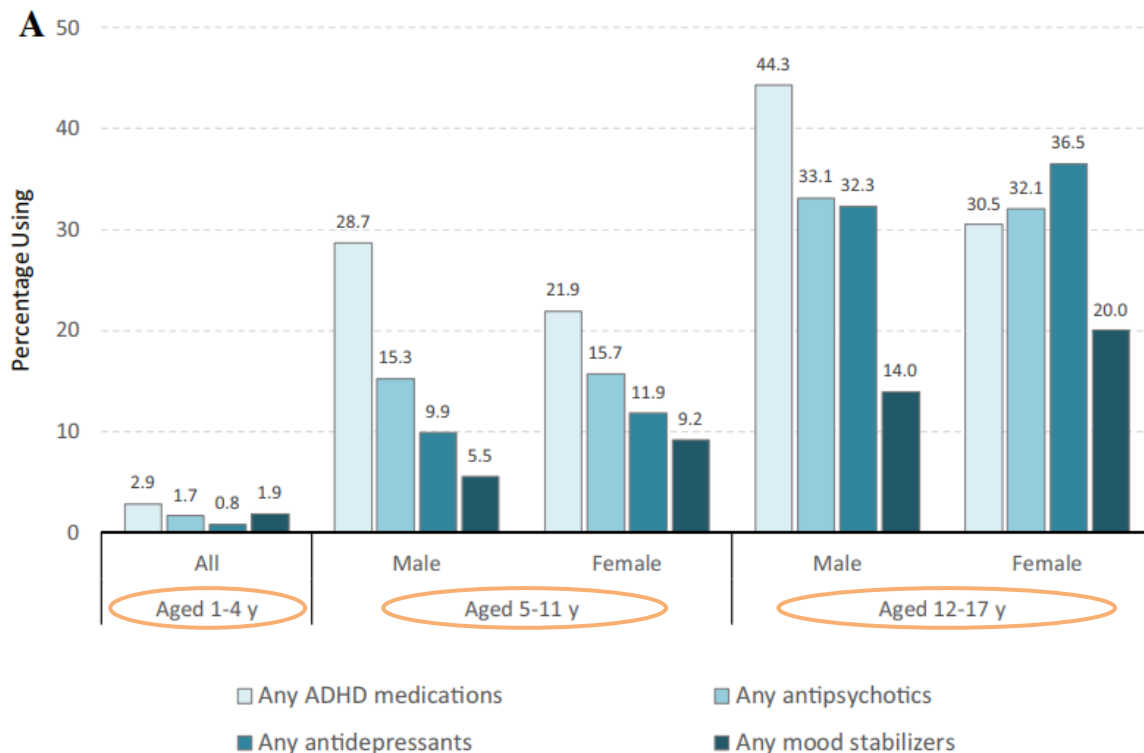
ASD cohort N = 7901; no-ASD cohort N = 79,010. Medication months supplied are added across all dispensings in class

^aOther ADHD medications included alpha-2 adrenergic agonists and norepinephrine reuptake inhibitors (see online appendix). Logistic regression models controlled for SES (neighborhood education attainment and median household income quartile), age, sex, and health system site





Fig. 2 Prevalence of use of psychotropic medication among children with ASD in 2010, comparing age and sex groups, by (a) major therapeutic class and (b) number of major classes ASD cohort N = 7901
Small cell count, <6 individuals



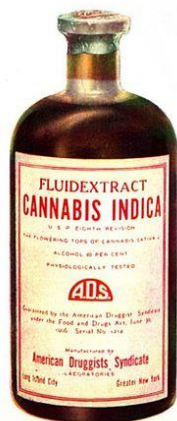


- פרט למאפייני הליבה של הפרעה יש גם: הפרעות התנהגות, היפראקטיביות, אגרסיה, התפרצויות, פגיעה עצמית, הפרעות בשינה.
- FDA-ריספרדל (RISPERIDONE) ואריפריפרזול (ARIPRAZOLE) מאושרים לשימוש בילדים הסובלים מאוטיזם עם אגרסיה ואי שקט – יש הוכחות מחקריות לגבי בטיחות ויעילות.
- מדווח בהפחתה של התנהגויות אגרסיביות, אי שקט, פגיעה עצמית וגם שיפור במאפייני ליבה (אך במידה מועטה).
- הפסקת הטיפול גורמת לחזרת הסימפטומים.
- המלצה: לטפל בתרופות אלו רק בילדים עם הפרעות התנהגות קשות ולא בכול ילד עם אבחנה של ASD.
- היפראקטיביות: ריטלין וסטימולנטים אחרים עוזרים, אך פחות מאשר ב ADHD רגיל. יש יותר הפסקות טיפול בגלל תופעות לוואי.
- הפרעות שינה – מלטונין רגיל ומלטונין בשחרור מושהה
- התנהגות חזרתית: אין הוכחות ליעילות SSRI's.





ומה לגבי קנאביס רפואי?



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ומה לגבי קנאביס רפואי?



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ClinicalTrials.gov

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input checked="" type="checkbox"/>	Completed	Cannabinoids for Behavioral Problems in Children With ASD	<ul style="list-style-type: none"> Autistic Disorder 	<ul style="list-style-type: none"> Drug: Cannabinoids - 99% pure cannabinoids mix Drug: Placebo Drug: Cannabinoids - whole plant extract 	<ul style="list-style-type: none"> Shaare Zedek Medical Center Jerusalem, Israel
2	<input checked="" type="checkbox"/>	Recruiting	Cannabidivarin (CBDV) vs. Placebo in Children With Autism Spectrum Disorder (ASD)	<ul style="list-style-type: none"> Autism Spectrum Disorder 	<ul style="list-style-type: none"> Drug: Cannabidivarin Drug: Matched Placebo 	<ul style="list-style-type: none"> Montefiore Medical Center Bronx, New York, United States



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- מופק מצמח, מוגדר כסם. בשימוש נרחב באופן חברתי (recreational drug), גם על ידי ילדים ונוער. מורכב מחומרים פעילים רבים, ביניהם כ-80-60 קנבינואידיים מוכרים, הידועים שבהם הם THC ו-CBD.

- קנאביס רפואי – THC נחשב למרכיב הפסיכו-אקטיבי החזק ביותר ול CBD מיוחסות התכונות הרפואיות. אינדיקציות - סרטן, מחלות מע' עיכול, תסמונות כאב, אפילפסיה עמידה ועוד. תכשירים - שמן, עישון, משאפים, עוגיות.



- קנאביס ופסיכיאטריה בישראל – מאושר לשימוש ב PTSD במבוגרים.
- קנאביס רפואי בילדים – מאושר לשימוש בסרטן, אפילפסיה, לאחרונה גם לאוטיזם.
- קימת ספרות מחקרית משמעותית, על בסיס של סדרות גדולות ומבוקרות היטב, המבססות סיכון משמעותי לנזקים פסיכיאטריים לשימוש ממושך בקנאביס בפרט בנוער. התחומים שבהם יש עדויות לנזק כוללים: פגיעה ביכולות הקוגניטיביות, במוטיבציה והעלאת הסיכון לפסיכוזה (Volkow, Swanson et al. 2016), העלאת הסיכון לחרדה ודכאון וכמו גם קשר לעליה באובדנות, בפרט במתבגרים שהשתמשו בקנאביס (Gobbi, Atkin et al. 2019).
- יש חשיבות למודעות לכך שאין מידע על שימוש מתמשך בקנאביס בילדים.





- קיים מעט מאוד מחקר קליני, יש דיווחים ראשוניים על בטיחות ויעילות במחקרי סקירה ו case reports, אך למרות שימוש נרחב יחסית, הבסיס המדעי חלקי בלבד ואין עדיין מחקרים גדולים כפולי סמיות לגבי בטיחות ויעילות. כרגע מתקיימים מחקרים בודדים בעולם, אחד בארץ ב"שערי צדק" (עדי ארן), אחד בניו-יורק.





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ClinicalTrials.gov

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Unknown †	Autologous Bone Marrow Stem Cells for Children With Autism Spectrum Disorders	<ul style="list-style-type: none"> Autism Autism Spectrum 	<ul style="list-style-type: none"> Other: Stem cells 	<ul style="list-style-type: none"> Hematology Service, Hospital Universitario Dr. Jose E. Gonzalez Monterrey, Nuevo Leon, Mexico
2	<input type="checkbox"/>	Completed	Safety and Efficacy of Stem Cell Therapy in Patients With Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Biological: human cord blood mononuclear cells Biological: human cord blood mononuclear cells and human umbilical cord mesenchymal stem cells 	<ul style="list-style-type: none"> Shandong Jiaotong Hospital Jinan, Shandong, China
3	<input type="checkbox"/>	Completed	Autologous Bone Marrow Stem Cell Therapy for Autism	<ul style="list-style-type: none"> Autistic Disorder 	<ul style="list-style-type: none"> Biological: Autologous Bone Marrow Mononuclear Cells 	<ul style="list-style-type: none"> Vinmec International Hospital Hanoi, Vietnam
4	<input type="checkbox"/>	Completed	Allogeneic Umbilical Cord Mesenchymal Stem Cell Therapy for Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Biological: Umbilical cord mesenchymal stem cells 	<ul style="list-style-type: none"> Stem Cell Institute Panama City, Panama
5	<input type="checkbox"/>	Completed	Autologous Bone Marrow Stem Cell Therapy Combined With Psychological Therapy and Rehabilitation for Autism	<ul style="list-style-type: none"> Stem Cell Transplantation 	<ul style="list-style-type: none"> Biological: Stem cell transplantation Behavioral: Psychological therapy and Rehabilitation 	<ul style="list-style-type: none"> Vinmec Research Institute of Stem Cell and Gene Technology Hanoi, Vietnam
6	<input type="checkbox"/>	Completed Has Results	Autologous Cord Blood Stem Cells for Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Biological: Autologous Cord Blood Stem Cells Biological: Placebo 	<ul style="list-style-type: none"> Sutter Pediatric Neurology Sacramento, California, United States
7	<input type="checkbox"/>	Withdrawn	Adipose Derived Stem Cell Therapy for Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Procedure: Fat Harvesting and Stem Cell Injection 	<ul style="list-style-type: none"> Ageless Regenerative Institute LLC Aventura, Florida, United States
8	<input type="checkbox"/>	Withdrawn	Stem Cell Therapy in Autism Spectrum Disorders	<ul style="list-style-type: none"> Autism Spectrum Disorders 	<ul style="list-style-type: none"> Procedure: Autologous bone marrow mononuclear cell transplantation 	<ul style="list-style-type: none"> Neurogen brain and spine institute Mumbai, Maharashtra, India





Safety and Observations from a Placebo-Controlled, Crossover Study to Assess Use of Autologous Umbilical Cord Blood Stem Cells to Improve Symptoms in Children with Autism

MICHAEL CHEZ,^{a,b} CHRISTOPHER LEPAGE,^{a,b} CAROL PARISE ,^b ASHLEY DANG-CHU,^b ANDREA HANKINS,^b MICHAEL CARROLL^c

Key Words. Stem cells • Umbilical cord blood • Autologous • Clinical trials • Autism • Language tests

ABSTRACT

The aim of this exploratory study was to assess the safety and clinical effects of autologous umbilical cord blood (AUCB) infusion in children with idiopathic autism spectrum disorder (ASD). Twenty-nine children 2 to 6 years of age with a confirmed diagnosis of ASD participated in this randomized, blinded, placebo-controlled, crossover trial. Participants were randomized to receive AUCB or placebo, evaluated at baseline, 12, and 24 weeks, received the opposite infusion, then re-evaluated at the same time points. Evaluations included assessments of safety, Expressive One Word Picture Vocabulary Test, 4th edition, Receptive One Word Picture Vocabulary Test, 4th edition, Clinical Global Impression, Stanford-Binet Fluid Reasoning and Knowledge, and the Vineland Adaptive Behavior and Socialization Subscales. Generalized linear models were used to assess the effects of the response variables at the 12- and 24-week time periods under each condition (AUCB, placebo). There were no serious adverse events. There were trends toward improvement, particularly in socialization, but there were no statistically significant differences for any endpoints. The results of this study suggest that autologous umbilical cord infusions are safe for children with ASD. Tightly controlled trials are necessary to further progress the study of AUCB for autism. *STEM CELLS TRANSLATIONAL MEDICINE* 2018;7:333–341

"לא היה הבדל
משמעותי סטטיסטית
באף אחת מנקודות
הסיום"








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ClinicalTrials.gov

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Completed	Allogeneic Umbilical Cord Mesenchymal Stem Cell Therapy for Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Biological: Umbilical cord mesenchymal stem cells 	<ul style="list-style-type: none"> Stem Cell Institute Panama City, Panama
2	<input type="checkbox"/>	Completed	Autologous Umbilical Cord Blood Infusion for Children With Autism Spectrum Disorder (ASD)	<ul style="list-style-type: none"> Autism Spectrum Disorder 	<ul style="list-style-type: none"> Biological: Autologous Umbilical Cord Blood 	<ul style="list-style-type: none"> Duke University Medical Center Durham, North Carolina, United States
3	<input type="checkbox"/>	Not yet recruiting NEW	Treatment of Children With Autistic Spectrum Disorder With Autologous Umbilical Cord Blood, a Pilot Study	<ul style="list-style-type: none"> Autistic Spectrum Disorder 	<ul style="list-style-type: none"> Biological: Autologous umbilical cord blood Biological: Placebo 	
4	<input type="checkbox"/>	Enrolling by invitation	Allogenic Cord Blood Transfusion in Patients With Autism	<ul style="list-style-type: none"> Autism Spectrum Disorder Autism 	<ul style="list-style-type: none"> Biological: ASD CB-MNC injection. Other: Standard therapy. 	<ul style="list-style-type: none"> Medical Centre Dinasty Samara, Russian Federation
5	<input type="checkbox"/>	Recruiting	hCT-MSC in Children With Autism Spectrum Disorder	<ul style="list-style-type: none"> Autism Autism Spectrum Disorder 	<ul style="list-style-type: none"> Biological: Cord Tissue Mesenchymal Stromal Cells Other: Placebo infusion 	<ul style="list-style-type: none"> Duke University Medical Center Durham, North Carolina, United States
6	<input type="checkbox"/>	Recruiting	Safety and Efficacy of the Transfusion of UCB in Patients With an ASD Depending on the Degree of HLA Compatibility	<ul style="list-style-type: none"> Autism Spectrum Disorder Autism 	<ul style="list-style-type: none"> Biological: ASD CB-MNC infusion low level HLA compatibility. Biological: ASD CB-MNC infusion high level HLA compatibility. Other: Standard therapy. 	<ul style="list-style-type: none"> Medical Centre Dinasty Samara, Russian Federation
7	<input type="checkbox"/>	Completed Has Results	Autologous Cord Blood Stem Cells for Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Biological: Autologous Cord Blood Stem Cells Biological: Placebo 	<ul style="list-style-type: none"> Sutter Pediatric Neurology Sacramento, California, United States
8	<input type="checkbox"/>	Completed Has Results	Cord Blood Infusion for Children With Autism Spectrum Disorder	<ul style="list-style-type: none"> Autism Spectrum Disorder ASD Autism PDD 	<ul style="list-style-type: none"> Biological: Cord Blood Infusion Biological: Placebo 	<ul style="list-style-type: none"> Duke University Medical Center Durham, North Carolina, United States
9	<input type="checkbox"/>	Completed	hCT-MSCs for Children With Autism Spectrum Disorder (ASD)	<ul style="list-style-type: none"> Autism Autism Spectrum Disorder ASD 	<ul style="list-style-type: none"> Biological: hCT-MSC infusion 	<ul style="list-style-type: none"> Duke University Medical Center Durham, North Carolina, United States
10	<input type="checkbox"/>	Enrolling by invitation	Oxytocin Versus Cord Blood for Improving Autistic Disorder	<ul style="list-style-type: none"> Autistic Spectrum Disorder 	<ul style="list-style-type: none"> Drug: Intranasal oxytocin Biological: Autologous umbilical cord blood 	<ul style="list-style-type: none"> Spitalul Angliomedica Bucharest, Bucuresti, Romania
11	<input type="checkbox"/>	Recruiting	Umbilical Cord Milking in Non-Vigorous Infants Developmental Followup (MINVIFU)	<ul style="list-style-type: none"> Neurodevelopmental Abnormality 	<ul style="list-style-type: none"> Procedure: Umbilical Cord Milking Procedure: Early Cord Clamping 	<ul style="list-style-type: none"> University of California, Davis Davis, California, United States Loma Linda Medical Center Loma Linda, California, United States Sharp Grossmont Hospital San Diego, California, United States (and 7 more...)
12	<input type="checkbox"/>	Not yet recruiting	Umbilical Cord Milking in Neonates Who Are Depressed at Birth-Developmental Follow Up (MIDAB-FU)	<ul style="list-style-type: none"> Hypoxic-Ischemic Encephalopathy Birth Asphyxia 	<ul style="list-style-type: none"> Other: Umbilical Cord Milking 	<ul style="list-style-type: none"> Daga Memorial Woman and Children Hospital Nagpur, MS, India Government Medical College and Hospital Nagpur, MS, India NKP Salve Institute of Medical Sciences and Lata Mangeshkar Hospital Nagpur, MS, India
13	<input type="checkbox"/>	Enrolling by invitation	Allogenic Cord Blood Transfusion in Patients With Cerebral Palsy	<ul style="list-style-type: none"> Cerebral Palsy 	<ul style="list-style-type: none"> Biological: CP CB-MNC injection Other: Standard therapy 	<ul style="list-style-type: none"> Medical Centre Dinasty Samara, Russian Federation
14	<input type="checkbox"/>	Recruiting	Feasibility and Safety of Umbilical Cord Blood Transfusion in the Treatment of Neonatal Cerebral Ischemia and Anemia	<ul style="list-style-type: none"> Hypoxic-Ischemic Encephalopathy Hypoxia Neonatal 	<ul style="list-style-type: none"> Biological: autologous umbilical cord blood (UCB) Procedure: standard care 	<ul style="list-style-type: none"> The Chinese University of Hong Kong Sha Tin, Hong Kong



White Matter Tract Changes Associated with Clinical Improvement in an Open-Label Trial Assessing Autologous Umbilical Cord Blood for Treatment of Young Children with Autism

KIMBERLY L. H. CARPENTER ^a, SAMANTHA MAJOR,^a CATHERINE TALLMAN,^b LYON W. CHEN,^b LAUREN FRANZ,^{a,c} JESSICA SUN ^d, JOANNE KURTZBERG,^d ALLEN SONG,^b GERALDINE DAWSON ^{a,d}

Key Words. Autism spectrum disorder • Autologous umbilical cord blood • White matter connectivity • Diffusion tensor imaging

ABSTRACT

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by social communication deficits and the presence of restricted interests and repetitive behaviors. We have previously reported significant improvements in behavior, including increased social functioning, improved communication abilities, and decreased clinical symptoms in children with ASD, following treatment with a single infusion of autologous cord blood in a phase I open-label trial. In the current study, we aimed to understand whether these improvements were associated with concurrent changes in brain structural connectivity. Twenty-five 2- to 6-year-old children with ASD participated in this trial. Clinical outcome measures included the Vineland Adaptive Behavior Scales-II Socialization Subscale, Expressive One-Word Picture Vocabulary Test-4, and the Clinical Global Impression-Improvement Scale. Structural connectivity was measured at baseline and at 6 months in a subset of 19 children with 25-direction diffusion tensor imaging and deterministic tractography. Behavioral improvements were associated with increased white matter connectivity in frontal, temporal, and subcortical regions (hippocampus and basal ganglia) that have been previously shown to show anatomical, connectivity, and functional abnormalities in ASD. The current results suggest that improvements in social communication skills and a reduction in symptoms in children with ASD following treatment with autologous cord blood infusion were associated with increased structural connectivity in brain networks supporting social, communication, and language abilities. *STEM CELLS TRANSLATIONAL MEDICINE 2019;8:138–147*

"בעקבות הטיפול היה שיפור בתקשורת חברתית והפחתה בסימפטומים. במח הודגמו שינויים חיוביים בחומר הלבן של שיפור במוליכות בין אזורים שונים, בהתאמה לממצאים הקליניים"





טיפול באוקסיטוצין



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Displaying 1-20 of 20 studies (20 studies per page)

How	Study Status	Study Title	Conditions	Interventions	Locations
1	Completed	Study of Oxytocin in Autism to Increase Interpersonal Social Interactions	Autism Spectrum Disorders	<ul style="list-style-type: none"> Drug: Placebo Nasal Spray Drug: Oxytocin Nasal Spray 	<ul style="list-style-type: none"> Little Center for Autism, Massachusetts General Hospital Boston, Massachusetts, United States Mount Sinai School of Medicine New York, New York, United States Center for Autism and the Developing Brain White Plains, New York, United States (and 4 more...)
2	Withdrawn	Intranasal Oxytocin and Learning in Autism	Autism Spectrum Disorders	<ul style="list-style-type: none"> Drug: Syntocinon (synthetic oxytocin) Other: Placebo 	<ul style="list-style-type: none"> Center for Neurobehavioral Development Minneapolis, Minnesota, United States
3	Completed View Results	Intranasal Oxytocin Treatment for Social Deficits in Children With Autism	Autism	<ul style="list-style-type: none"> Drug: Oxytocin nasal spray Drug: Placebo 	<ul style="list-style-type: none"> Stanford University School of Medicine Stanford, California, United States
4	Completed View Results	A Study of Oxytocin in Children and Adolescents With Autistic Disorder	Autism	<ul style="list-style-type: none"> Drug: Oxytocin Drug: Placebo 	<ul style="list-style-type: none"> University of North Carolina Chapel Hill Chapel Hill, North Carolina, United States
5	Completed View Results	Intranasal Oxytocin and Learning in Autism	Autism Spectrum Disorders	<ul style="list-style-type: none"> Drug: Intranasal Oxytocin (Trade name: Syntocinon) 	<ul style="list-style-type: none"> The Children's Hospital of Philadelphia Philadelphia, Pennsylvania, United States
6	Completed	Intranasal Oxytocin for the Treatment of Children and Adolescents With Autism Spectrum Disorders (ASD)	Autism Spectrum Disorder	<ul style="list-style-type: none"> Drug: Intranasal Oxytocin Drug: Placebo 	<ul style="list-style-type: none"> University of Minnesota Minneapolis, Minnesota, United States Holland Bloorview Kids Rehabilitation Hospital Toronto, Ontario, Canada
7	Completed	Oxytocin in Spectrum Autism Disorders	Autistic Disorder	<ul style="list-style-type: none"> Drug: Oxytocin Other: placebo 	<ul style="list-style-type: none"> Instituto de Psiquiatria São Paulo, Brazil
8	Completed View Results	Intranasal Oxytocin for the Treatment of Children and Adolescents With ASD (OXY)	Autism Spectrum Disorder	<ul style="list-style-type: none"> Drug: Intranasal Oxytocin 	<ul style="list-style-type: none"> Holland Bloorview Kids Rehabilitation Hospital Toronto, Ontario, Canada
9	Recruiting	Oxytocin and Social Cognitive Skills Group	Autism Spectrum Disorder	<ul style="list-style-type: none"> Drug: Oxytocin and social cognitive skills group Behavioral: Facilitated Play Therapy 	<ul style="list-style-type: none"> Rush University Medical Center Chicago, Illinois, United States
10	Enrolling by invitation	Oxytocin Nasal Spray Used for Improving Autistic Disorder	Autistic Disorder	<ul style="list-style-type: none"> Drug: Intranasal oxytocin Biological: Autologous umbilical cord blood 	<ul style="list-style-type: none"> Spiridul Angromedica Bucharest, Bucharest, Romania
11	Completed	Open Randomized Trial of Intranasal Oxytocin Treatment in Autism	Autism Spectrum Disorders	<ul style="list-style-type: none"> Drug: Oxytocin 	<ul style="list-style-type: none"> The University of North Carolina at Chapel Hill Chapel Hill, North Carolina, United States
12	Active, not recruiting	An Open-label Trial of Oxytocin in Adolescents With Autism Spectrum Disorders	<ul style="list-style-type: none"> Autism Spectrum Disorders Personality Developmental Disorders ASD PDD 	<ul style="list-style-type: none"> Drug: Intranasal Oxytocin 	<ul style="list-style-type: none"> Massachusetts General Hospital Boston, Massachusetts, United States
13	Terminated	Oxytocin in Adolescents With Autism Spectrum Disorders	Autism Spectrum Disorder	<ul style="list-style-type: none"> Drug: OXYTOCINA - SHIRAY NASAL 	<ul style="list-style-type: none"> Instituto de Psiquiatria, Clinical Hospital at São Paulo São Paulo, Brazil
14	Withdrawn	Facile Interactions of Parents With Autism and Oxytocin	Autism Disorder	<ul style="list-style-type: none"> Drug: Oxytocin Drug: Placebo nasal spray 	<ul style="list-style-type: none"> University of California, San Francisco San Francisco, California, United States
15	Active, not recruiting	Open Study of Intranasal Oxytocin and Parental Effects in Autism	Autism Spectrum Disorders	<ul style="list-style-type: none"> Drug: Intranasal Oxytocin Drug: Placebo 	<ul style="list-style-type: none"> Center for Neurobehavioral Development Minneapolis, Minnesota, United States
16	Active, not recruiting	Vaginal and Oxytocin Nasal Spray on Social Behavioral Autism Spectrum Disorder (ASD) Children	Autism Spectrum Disorder	<ul style="list-style-type: none"> Drug: Intranasal oxytocin Dietary Supplement: oral probiotics Dietary Supplement: oral placebo 	<ul style="list-style-type: none"> Massachusetts General Hospital Charlestown, Massachusetts, United States
17	Active, not recruiting	A Study of Oxytocin for the Treatment of Social Impairment in Individuals with High Functioning Autism Spectrum Disorders	<ul style="list-style-type: none"> Autism Spectrum Disorder Personality Developmental Disorder ASD PDD 	<ul style="list-style-type: none"> Drug: Intranasal Oxytocin 	<ul style="list-style-type: none"> Massachusetts General Hospital Boston, Massachusetts, United States
18	Recruiting	Translating Neuroimaging into Diagnostic Markers Via Brain Drains	Autism Spectrum Disorder	<ul style="list-style-type: none"> Drug: Oxytocin Behavioral: Prolonged Response Treatment Drug: Placebo 	<ul style="list-style-type: none"> Yale School of Medicine New Haven, Connecticut, United States
19	Recruiting	Effects of Oxytocin-Ultrasound Frequencies on Behavioral and Neural Responses	Healthy	<ul style="list-style-type: none"> Drug: Nasal Sprays 	<ul style="list-style-type: none"> school of life science and technology, University of Electronic Science and Technology of China Chengdu, Sichuan, China
20	Completed View Results	The Role of Vasopressin in the Social Deficits of Autism	Autism Spectrum Disorders	<ul style="list-style-type: none"> Drug: Vasopressin Drug: Placebo 	<ul style="list-style-type: none"> Stanford University School of Medicine, Psychiatry and Behavioral Sciences Stanford, California, United States



The effects of a course of intranasal oxytocin on social behaviors in youth diagnosed with autism spectrum disorders: a randomized controlled trial

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Bruce J. Tonge,² Ian B. Hickie,¹ Caroline M. Keating,² Cristina Cacciotti-Saija,¹
and Stewart L. Einfeld^{1,4}

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Background: There is increasing interest in oxytocin as a therapeutic to treat social deficits in autism spectrum disorders (ASD). The aim of this study was to investigate the efficacy of a course of oxytocin nasal spray to improve social behavior in youth with ASD. **Methods:** In a double-blind, placebo-controlled trial across two Australian university sites between February 2009 and January 2012, 50 male participants aged between 12 and 18 years, with Autistic or Asperger's Disorder, were randomized to receive either oxytocin ($n = 26$) or placebo ($n = 24$) nasal sprays (either 18 or 24 International Units), administered twice-daily for 8 weeks. Participants were assessed at baseline, after 4- and 8-weeks of treatment, and at 3-month follow-up. Primary outcomes were change in total scores on the caregiver-completed Social Responsiveness Scale and clinician-ratings on the Clinical Global Impressions-Improvement scale. Secondary assessments included caregiver reports of repetitive and other developmental behaviors and social cognition. Clinical trial registration: Australian New Zealand Clinical Trials Registry www.anzctr.org.au ACTRN12609000513213. **Results:** Participants who received oxytocin showed no benefit following treatment on primary or secondary outcomes. However, caregivers who believed their children received oxytocin reported greater improvements compared to caregivers who believed their child received placebo. Nasal sprays were well tolerated and there was no evidence of increased side effects resulting from oxytocin administration. **Conclusions:** This is the first evaluation of the efficacy for a course of oxytocin treatment for youth with ASD. Although results did not suggest clinical efficacy, further research is needed to explore alternative delivery methods, earlier age of intervention, and the influence of caregiver expectation on treatment response. **Keywords:** Social cognition, neuropeptides, developmental disorder, emotion recognition, placebo-controlled.

"ללא השפעה על
תקשורת חברתית
במתבגרים"



Review

Social Interaction Improved by Oxytocin in the Subclass of Autism with Comorbid Intellectual Disabilities

Haruhiro Higashida ^{1,*}, Toshio Munosue ¹, Hiroataka Kosaka ², Hidenori Yamasue ³, Shigeru Yokoyama ¹ and Mitsuru Kikuchi ¹

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Abstract: Approximately half of all autism spectrum disorder (ASD) individuals suffer from comorbid intellectual disabilities. Furthermore, the prevalence of epilepsy has been estimated to be 46% of patients with low intelligence quotient. It is important to investigate the therapeutic benefits and adverse effects of any recently developed drugs for this proportion of individuals with the so-called Kanner type of ASD. Therefore, we investigated the therapeutic and/or adverse effects of intranasal oxytocin (OT) administration, especially in adolescents and adults with ASD and comorbid intellectual disability and epilepsy, with regard to core symptoms of social deficits. We have already reported three randomized placebo-controlled trials (RCTs). However, we revisit results in our pilot studies from the view of comorbidity. Most of the intellectually disabled participants were found to be feasible participants of the RCT. We observed significantly more events regarded as reciprocal social interaction in the OT group compared with the placebo group. In the trial, no or little differences in adverse events were found between the OT and placebo arms, as found in some other reports. However, seizures were induced in three participants with medical history of epilepsy during or after OT treatment. In conclusion, we stress that behavioral changes in ASD patients with intellectual disabilities could be recognized not by the conventional measurements of ASD symptoms but by detailed evaluation of social interactions arising in daily-life situations.

Keywords: autism; oxytocin; subclasses; intellectual disability; epilepsy; randomized controlled trial

"מאמר סקירה -
השפעה מיטיבה
ביחס לפלסבו על
תקשורת חברתית
במתבגרים עם
אוטיזם ומוגבלות
שכלית"



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Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Completed	Therapeutic Issues for Autism	<ul style="list-style-type: none"> Autism Spectrum Disorder 	<ul style="list-style-type: none"> Drug: Risperidone Device: hyperbaric oxygen therapy Drug: Non specific Multivitamin 	
2	<input type="checkbox"/>	Completed Has Results	Pilot Study of the Effect of Hyperbaric Oxygen Treatment on Behavioral and Biomarker Measures in Children With Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Other: Hyperbaric Oxygen Treatment (HBOT) 	
3	<input type="checkbox"/>	Completed	A Clinical Trial of the Clinical Effects of Hyperbaric Oxygen Therapy in Thai Autistic Children	<ul style="list-style-type: none"> Autistic Disorder 	<ul style="list-style-type: none"> Procedure: oxygen (Hyperbaric Oxygen Therapy) 	<ul style="list-style-type: none"> Vachira Phuket Hospital Phuket, Thailand
4	<input type="checkbox"/>	Completed	Effects of Hyperbaric Oxygen Therapy on Children With Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Device: Hyperbaric Oxygen Therapy 	<ul style="list-style-type: none"> Medical Center at Thoughtful House Austin, Texas, United States
5	<input type="checkbox"/>	Unknown †	Effects of Hyperbaric Oxygen Therapy on Cognitive Function on Autistic Spectrum Disordered Children	<ul style="list-style-type: none"> Cognition 	<ul style="list-style-type: none"> Procedure: Hyperbaric oxygen therapy 	<ul style="list-style-type: none"> Pediatric Partners of Ponte Vedra Ponte Vedra Beach, Florida, United States
6	<input type="checkbox"/>	Completed	Effect of Hyperbaric Therapy on Markers of Oxidative Stress in Children With Autism	<ul style="list-style-type: none"> Autism Oxidative Stress 	<ul style="list-style-type: none"> Other: Hyperbaric Oxygen 	<ul style="list-style-type: none"> ICDRC Melbourne, Florida, United States
7	<input type="checkbox"/>	Completed	A Controlled Trial of the Clinical Effects of Hyperbaric Therapy in Autistic Children	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Procedure: Hyperbaric Therapy 	<ul style="list-style-type: none"> Center for Autism Research and Education Phoenix, Arizona, United States International Child Development Resource Center Melbourne, Florida, United States Blue Ridge Spectrum Center Charlottesville, Virginia, United States Advocates for Children Lynchburg, Virginia, United States



Research article

Open Access

Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial

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Gregg Hintz - therapeuticpathways@yahoo.com; Barry Grushkin - bgrushkin2@cs.com; Elizabeth A Mumper - drmumper@rimlandcenter.com

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Accepted: 13 March 2009

"טיפול בתא לחץ בחמצן
בריכוז 24%, בלחץ של 1.3
אטמוספרות, גרם לשיפור
קליני משמעותי בהבנת שפה,
תקשורת חברתית וקשר עין
בילדים עם אוטיזם"

Conclusion: Children with autism who received hyperbaric treatment at 1.3 atm and 24% oxygen for 40 hourly sessions had significant improvements in overall functioning, receptive language, social interaction, eye contact, and sensory/cognitive awareness compared to children who received slightly pressurized room air.



Research in Autism Spectrum Disorders 4 (2010) 268–275



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Randomized trial of hyperbaric oxygen therapy for children with autism

Doreen Granpeesheh^a, Jonathan Tarbox^a, Dennis R. Dixon^{a,*}, Arthur E. Wilke^a, Michael S. Allen^a, James Jeffrey Bradstreet^b

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ARTICLE INFO

Keywords:

Autism Spectrum Disorders
Autism Treatment
Hyperbaric oxygen therapy
Applied behavior analysis

ABSTRACT

Autism Spectrum Disorders (ASDs) are characterized by the presence of impaired development in social interaction and communication and the presence of a restricted repertoire of activity and interests. While numerous treatments for ASDs have been proposed, very few have been subjected to rigorous scientific investigation. Hyperbaric oxygen therapy (HBOT) has been recently popularized as a treatment for the symptoms of ASDs. The purpose of this study was to test the hypothesis that HBOT would have a beneficial effect on ASD symptoms in the context of a double-blind placebo-controlled trial. This randomized double-blind placebo-controlled trial compared HBOT used to deliver 24% oxygen at 1.3 atmospheric pressure ($n = 18$) to placebo ($n = 16$) in children with Autistic Disorder. Both direct observational measures of behaviors symptomatic of autism and standardized psychological assessments were used to evaluate the effects of the treatment. No differences were detected between HBOT and placebo groups across any of the outcome measures. The present study demonstrates that HBOT delivered at 24% oxygen at 1.3 atmospheric pressure does not result in a clinically significant improvement of the symptoms of Autistic Disorder.

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בחמצן בריכוז 24%
בלחץ של 1.3
אטמוספרות לא גרם
לשיפור קליני
בסימפטומים של
אוטיזם"



טיפול בדיאטות מיוחדות



Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Unknown †	Gluten for Autism Spectrum Disorders	<ul style="list-style-type: none"> Autism Spectrum Disorders 	<ul style="list-style-type: none"> Other: Gluten challenge 	<ul style="list-style-type: none"> Medical University of Warsaw Warsaw, Poland
2	<input type="checkbox"/>	Completed Has Results	ScanBrit Dietary Intervention in Autism	<ul style="list-style-type: none"> Autism Autism Spectrum Disorder (ASD) 	<ul style="list-style-type: none"> Other: Gluten- and casein-free diet 	
3	<input type="checkbox"/>	Active, not recruiting NEW	Dates as a Functional Food for Autism	<ul style="list-style-type: none"> Autistic Spectrum Disorder 	<ul style="list-style-type: none"> Other: Dates fruit as functional Food Behavioral: behavioral modification and stimulation Other: nutritional Guidance 	<ul style="list-style-type: none"> National Research Centre Giza, Al Jizah, Egypt
4	<input type="checkbox"/>	Completed	A Study to Assess the Role of a Gluten Free-dairy Free (GFCF) Diet in the Dietary Management of Autism Associated Gastrointestinal Disorders	<ul style="list-style-type: none"> Autism Gastrointestinal Symptoms 	<ul style="list-style-type: none"> Other: GFCF product with GFCF diet Other: product containing gluten and casein (milk protein) with GFCF diet 	<ul style="list-style-type: none"> Massachusetts General Hospital Boston, Massachusetts, United States Baylor College of Medicine / Texas Children's Hospital Houston, Texas, United States
5	<input type="checkbox"/>	Completed	Diet and Behavior in Young Children With Autism	<ul style="list-style-type: none"> Autism Autistic Disorder 	<ul style="list-style-type: none"> Behavioral: Gluten- and casein-free diet Behavioral: Placebo controlled diet 	<ul style="list-style-type: none"> University of Rochester Medical Center Rochester, New York, United States
6	<input type="checkbox"/>	Completed	Nutritional and Dietary Treatment Study for Children/Adults With Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Dietary Supplement: Nutritional and Dietary Interventions 	<ul style="list-style-type: none"> Arizona State University Tempe, Arizona, United States
7	<input type="checkbox"/>	Completed	Pilot Study of Diet and Behavior in Children With Autism	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Dietary Supplement: Gluten and dry milk Dietary Supplement: Placebo 	<ul style="list-style-type: none"> The University of Texas Health Science Center At Houston Houston, Texas, United States



[Nutr Neurosci](#). 2010 Apr;13(2):87-100. doi: 10.1179/147683010X12611460763922.

The ScanBrit randomised, controlled, single-blind study of a gluten- and casein-free dietary intervention for children with autism spectrum disorders.

[Whiteley P¹](#), [Haracopos D](#), [Knivsberg AM](#), [Reichelt KL](#), [Parlar S](#), [Jacobsen J](#), [Seim A](#), [Pedersen L](#), [Schondel M](#), [Shattock P](#)

Ⓜ Author information

Abstract

There is increasing interest in the use of gluten- and casein-free diets for children with autism spectrum disorders (ASDs). We report results from a two-stage, 24-month, randomised, controlled trial incorporating an adaptive 'catch-up' design and interim analysis. Stage 1 of the trial saw 72 Danish children (aged 4 years to 10 years 11 months) assigned to diet (A) or non-diet (B) groups by stratified randomisation. Autism Diagnostic Observation Schedule (ADOS) and the Gilliam Autism Rating Scale (GARS) were used to assess core autism behaviours, Vineland Adaptive Behaviour Scales (VABS) to ascertain developmental level, and Attention-Deficit Hyperactivity Disorder - IV scale (ADHD-IV) to determine inattention and hyperactivity. Participants were tested at baseline, 8, and 12 months. Based on per protocol repeated measures analysis, data for 26 diet children and 29 controls were available at 12 months. At this point, there was a significant improvement to mean diet group scores (time*treatment interaction) on sub-domains of ADOS, GARS and ADHD-IV measures. Surpassing of predefined statistical thresholds as evidence of improvement in group A at 12 months sanctioned the re-assignment of group B participants to active dietary treatment. Stage 2 data for 18 group A and 17 group B participants were available at 24 months. Multiple scenario analysis based on inter- and intra-group comparisons showed some evidence of sustained clinical group improvements although possibly indicative of a plateau effect for intervention. Our results suggest that dietary intervention may positively affect developmental outcome for some children diagnosed with ASD. In the absence of a placebo condition to the current investigation, we are, however, unable to disqualify potential effects derived from intervention outside of dietary changes. Further studies are required to ascertain potential best- and non-responders to intervention. The study was registered with [ClinicalTrials.gov](#), number [NCT00614198](#).

"בדיאטת ללא
גלוטן וללא קזאין –
נצפה שיפור מסוים
שמתמתן עם
הזמן, לא נבדק
מול פלסבו"



Journal of Autism and Developmental Disorders, Vol. 36, No. 3, April 2006 (© 2006)

DOI 10.1007/s10803-006-0079-0

Published Online: March 23, 2006

The Gluten-Free, Casein-Free Diet In Autism: Results of A Preliminary Double Blind Clinical Trial

Jennifer Harrison Elder,^{1,3} Meena Shankar,² Jonathan Shuster,² Douglas Theriaque,² Sylvia Burns,¹ and Lindsay Sherrill¹

This study tested the efficacy of a gluten-free and casein-free (GFCF) diet in treating autism using a randomized, double blind repeated measures crossover design. The sample included 15 children aged 2–16 years with autism spectrum disorder. Data on autistic symptoms and urinary peptide levels were collected in the subjects' homes over the 12 weeks that they were on the diet. Group data indicated no statistically significant findings even though several parents reported improvement in their children. Although preliminary, this study demonstrates how a controlled clinical trial of the GFCF diet can be conducted, and suggests directions for future research.

KEY WORDS: Autism; diet; gluten; casein; GFCF diet.

"בדיאטת ללא
גלוטן וללא קזאין –
לא נצפו שינויים
משמעותיים
מבחינה
סטטיסטית"



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Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Terminated	Deep rTMS (Repetitive Transcranial Magnetic Stimulation) for Treatment of Autism Symptoms in Children.	<ul style="list-style-type: none"> Autism 	<ul style="list-style-type: none"> Device: Transcranial Magnetic Stimulation 	<ul style="list-style-type: none"> Hadassah Medical Organization Jerusalem, Israel
2	<input type="checkbox"/>	Completed	rTMS for Executive Function Deficits in Autism Spectrum Disorder	<ul style="list-style-type: none"> Autism Spectrum Disorder 	<ul style="list-style-type: none"> Device: Repetitive Transcranial Magnetic Stimulation 	<ul style="list-style-type: none"> Centre for Addictions and Mental Health Toronto, Ontario, Canada
3	<input type="checkbox"/>	Unknown †	Stimulant Autism Test	<ul style="list-style-type: none"> Autism Spectrum Disorder Attention Deficit Hyperactivity Disorder 	<ul style="list-style-type: none"> Drug: Methylphenidate Drug: Placebo 	<ul style="list-style-type: none"> Cincinnati Children's Hospital Medical Center Cincinnati, Ohio, United States
4	<input type="checkbox"/>	Recruiting	Effect of rTMS on the Abnormal Executive Function of ASD Children	<ul style="list-style-type: none"> Executive Dysfunction ASD 	<ul style="list-style-type: none"> Device: Active cTBS Device: Sham 	<ul style="list-style-type: none"> Fei Li Shanghai, Shanghai, China
5	<input type="checkbox"/>	Recruiting	From Molecules to Cognition: Inhibitory Mechanisms in ASD and NF1	<ul style="list-style-type: none"> Autism Spectrum Disorder Neurofibromatosis 1 	<ul style="list-style-type: none"> Drug: Lovastatin 60 MG Drug: Placebos 	<ul style="list-style-type: none"> ICNAS Coimbra, Portugal
6	<input type="checkbox"/>	Completed	Combined Treatment of Minocycline and Lovastatin to Treat Individuals With Fragile X Syndrome	<ul style="list-style-type: none"> Fragile X Syndrome 	<ul style="list-style-type: none"> Drug: Minocycline, then Minocycline/Lovastatin Drug: Lovastatin, then Minocycline/Lovastatin 	<ul style="list-style-type: none"> Centre de Recherche du CHUS Sherbrooke, Quebec, Canada



J Autism Dev Disord (2009) 39:619–634
DOI 10.1007/s10803-008-0662-7

ORIGINAL PAPER

Effects of Low Frequency Repetitive Transcranial Magnetic Stimulation (rTMS) on Gamma Frequency Oscillations and Event-Related Potentials During Processing of Illusory Figures in Autism

Estate M. Sokhadze · Ayman El-Baz · Joshua Baruth ·
Grace Mathai · Lonnie Sears · Manuel F. Casanova

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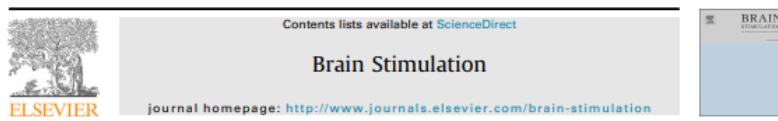
Abstract Previous studies by our group suggest that the neuropathology of autism is characterized by a disturbance of cortical modularity. In this model a decrease in the peripheral neuropil space of affected minicolumns provides for an inhibitory deficit and a readjustment in their signal to noise bias during information processing. In this study we proposed using low frequency transcranial magnetic stimulation (rTMS) as a way increasing the surround inhibition of minicolumns in autism. Thirteen patients (ADOS and ADI-R diagnosed) and equal number of controls participated in the study. Repetitive TMS was delivered at 0.5 Hz, 2 times per week for 3 weeks. Outcome measures based on event-related potentials (ERP), induced gamma activity, and behavioral measures showed

significant post-TMS improvement. The results suggest that rTMS offers a potential therapeutic intervention for autism.

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Treatment of Executive Function Deficits in autism spectrum disorder with repetitive transcranial magnetic stimulation: A double-blind, sham-controlled, pilot trial



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ABSTRACT

Background: In youth and young adults with autism spectrum disorder (ASD), executive function (EF) deficits may be a promising treatment target with potential impact on everyday functioning.
Objective: To conduct a pilot randomized, double-blind, parallel, controlled trial evaluating repetitive transcranial magnetic stimulation (rTMS) for EF deficits in ASD.
Method: In Toronto, Ontario (November 2014 to June 2017), a 20-session, 4-week course of 20 Hz rTMS targeting dorsolateral prefrontal cortex (DLPFC) (90%RMT) was compared to sham stimulation in 16–35 year-olds with ASD (28 male/12 female), without intellectual disability, who had impaired everyday EF performance (n = 20 active/n = 20 sham). Outcome measures evaluated protocol feasibility and clinical effects of active vs. sham rTMS on EF performance. The moderating effect of baseline functioning was explored.
Results: Of eligible participants, 95% were enrolled and 95% of randomized participants completed the protocol. Adverse events across treatment arms were mild-to-moderate. There was no significant difference between active vs. sham rTMS on EF performance. Baseline adaptive functioning moderated the effect of rTMS, such that participants with lower baseline functioning experienced significant EF improvement in the active vs. sham group.
Conclusions: Our pilot RCT demonstrated the feasibility and acceptability of using high frequency rTMS targeting DLPFC in youth and young adults with autism. No evidence for efficacy of active versus sham rTMS on EF performance was found. However, we found promising preliminary evidence of EF performance improvement following active versus sham rTMS in participants with ASD with more severe adaptive functioning deficits. Future work could focus on examining efficacy of rTMS in this higher-need population.
Clinical trial registration: Repetitive Transcranial Magnetic Stimulation (rTMS) for Executive Function Deficits in Autism Spectrum Disorder and Effects on Brain Structure: A Pilot Study; <https://clinicaltrials.gov/ct2/show/NCT02311751?term=ameis&rank=1>; NCT02311751. The trial was funded by an American Academy of Child and Adolescent Psychiatry (AACAP) Pilot Research Award, the Innovation Fund from the Alternate Funding Plan of the Academic Health Sciences Centres of Ontario, and an Ontario Mental Health Foundation (OMHF) Project A Grant and New Investigator Fellowship.
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"ללא שינוי סטטיסטי
בתפקודים ניהוליים בהשוואה
בין טיפול לפלסבו. שיפור
מסוים בתת קבוצה עם תפקוד
כללי נמוך יותר בתחילת
המחקר."



National Autism
Research Center
of Israel



לאורך השנים פותחו גישות טיפוליות שונות לאוטיזם. להלן רשימה חלקית של הטיפולים הנפוצים בישראל. חשוב לציין שבמקרים רבים, מטפלים משלבים עקרונות משיטות טיפול שונות כך שקשה להפריד בצורה נוקשה בין טיפולים בגישות השונות.

• **Applied Behavioral Analysis (ABA)**

גישה המבוססת על שינוי התנהגותי ומושגת על רעיונות מתחום הלמידה. השיטה כוללת עידוד התנהגויות רצויות לצד דיכוי התנהגויות לא רצויות. בנוסף מלמדים את הילד יכולות חדשות ומרחיבים את ההקשרים בהם משתמש הילד ביכולות אלה.

• **DIR | Floortime | Greenspan**

מודל המקדם את ההתפתחות של הילד על ידי יצירת אינטראקציה עם הורים ואחרים דרך משחק. המודל מתמקד במציאת מוקד העניין של הילד, ומאתגר את הילד להיות יצירתי וספונטני תוך עירוב החוויה החושית של הילד, יכולותיו המוטוריות ורגשותיו. מטרת המודל היא ליצור אינטראקציות רגשיות משמעותיות בין הדמות המטפלת והילד, על מנת לאפשר את התפתחותו בכל התחומים.

• **Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH)**

הגישה כוללת בנייה של תכנית עבודה אישית המותאמת לצרכיו של כל ילד בכל תחומי התפקוד. גישה זו משלבת הסתכלות התפתחותית עם טכניקות התנהגותיות (לדוגמה הבניית הסביבה) תוך מעורבות הורית רבה.

• **Early Start Denver Model (ESDM)**

היא שיטת התערבות המתאימה לילדים צעירים בני 12-48 חודשים שנבדקה באופן יחסית מקיף בכמה מחקרים ונמצאה כיעילה בקידום פעוטות עם אוטיזם. התוכנית מבוססת על עקרונות ה ABA תוך שימוש במצבים משחקיים ושימת דגש מיוחד על מערכת היחסים שנוצרת בין הילד והמטפל. מחקרים הראו כי השיטה משפרת את יכולות קוגניטיביות, שפתיות והתנהגות יומיומית של פעוטות עם אוטיזם.



- לא נמצא טיפול ביולוגי/תרופתי שמרפא אוטיזם.
- המנגנונים הביולוגיים באוטיזם אינם ידועים ברובם, מטרות המחקר לזהותם, לאתר את תת-הקבוצות ולהתאים טיפולים ספציפיים.
- טיפול תרופתי יכול להשתלב כחלק מהטיפול הכוללני.
- הטיפול התרופתי הקיים כיום הוא סימפטומטי ושמור למקרים ספציפיים.
- התערבויות וטיפולים פסיכולוגיים משפרים את מצב הילדים.
- אין עדות חד שמשמעות לעדיפות של שיטת טיפול מסוימת, אך קיימת הסכמה גורפת בין המטפלים והחוקרים שהתערבות אינטנסיבית ומוקדמת, שאינה תרופתית, משפרת את מצב הילדים.



תודה לילדים ולמשפחות





תודה לכל צוות מרכז המחקר



תודה על ההקשבה!

