**Supplementary Material**

**Cognitive, behavioral and socio-communication skills as predictors of response to Early Start Denver Model:**

**A prospective study in 32 young children with Autism Spectrum Disorder.**

**Lisa Asta1, Tiziana Di Bella2, Francesca La Fauci Belponer2, Marianna Bruschetta2, Silvia Martines2, Enrica Basile2, Maria Boncoddo3, Fabiana Bellomo2, Francesca Cucinotta4, Arianna Ricciardello2, Laura Turriziani5, Costanza Colombi6, Federico Banchelli7, Riccardo Cuoghi Costantini7, Roberto D'Amico7, Antonio M. Persico1,9\*.**

1 Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy,

2 Interdepartmental Program “Autism 0–90”, “G. Martino” University Hospital, Messina, Italy,

3 Institute for Biomedical Research and Innovation (IRIB), National Research Council of Italy (CNR), Messina, Italy,

4 IRCCS Centro Neurolesi "Bonino-Pulejo", Via Provinciale Palermo, Contrada Casazza, 98124 Messina, Italy

5 Center for Autism “Dopo di noi”, Barcellona Pozzo di Gotto, Messina, Italy,

6 IRCSS Stella Maris Foundation, Pisa, Italy,

7 Department of Medical and Surgical Sciences, University of Modena and Reggio Emilia, Modena, Italy,

8 Unit of Statistical and Methodological Support to Clinical Research, Modena University Hospital, Modena, Italy

9 Child and Adolescent Neuropsychiatry Program, Modena University Hospital, Modena, Italy

**Supplementary Table S1**. Mean (SD) pre-treatment (T0) and post-treatment (T2) scores. N=number of valid observations. Nominal one-tail p-values < 0.05 are highlighted in gray.

|  |  | **Pre-treatment (T0)** |  | **Post-treatment (T2)** | **Nominal*****p*-values** |
| --- | --- | --- | --- | --- | --- |
|  | ***N*** | **Mean (SD)** | **Range** | ***N*** | **Mean (SD)** | **Range** |
| **ADOS-2 Total score** | 24 | 17.83 (4.78) | 9-30 | 24 | 15.67 (5.12) | 6-23 | 0.02 |
| **ADOS-2 SA** | 24 | 14.96 (3.75) | 8-20 | 24 | 12.96 (4.71) | 3-19 | 0.01 |
| **ADOS-2 RRB** | 24 | 2.88 (2.19) | 0-10 | 24 | 2.71 (1.27) | 0-5 | 0.36 |
| **GMDS-ER GQ** | 32 | 60.8 (17.73) | 21-100 | 32 | 65.29 (17.89) | 43-111 | 0.04 |
| **GMDS-ER Locomotor** | 32 | 69.31 (21.13) | 24-124 | 32 | 73.25 (17.08) | 20-105 | 0.88 |
| **GMDS-ER Personal/Social** | 32 | 53.83 (17.22) | 19-99 | 32 | 59.69 (21.15) | 15-109 | 0.02 |
| **GMDS-ER Language** | 32 | 45.34 (18.26) | 14-103 | 32 | 50.15 (27.00) | 11-136 | 0.13 |
| **GMDS-ER Visuomotor Coordination** | 32 | 61.63 (20.11) | 17-103 | 32 | 64.75 (19.44) | 16-110 | 0.15 |
| **GMDS-ER Performance** | 31 | 71.09 (25.69) | 26-146 | 32 | 75.81 (26.01) | 17-125 | 0.19 |
| **PEP3 CVP** | 25 | 55.84 (18.37) | 32-110 | 24 | 67.11 (22.38) | 40-123 | 0.02 |
| **PEP-3 EL** | 25 | 43.36 (8.78) | 22-65 | 24 | 47.44 (18.98) | 25-83 | 0.20 |
| **PEP-3 RL** | 25 | 49.28 (14.57) | 22-79 | 24 | 56.01 (24.47) | 23-120 | 0.14 |
| **PEP-3 FM** | 25 | 65.92 (17.14) | 44-100 | 24 | 65.61 (11.35) | 44-88 | 0.70 |
| **PEP-3 GM** | 25 | 67.2 (17.16) | 44-103 | 24 | 67.64 (16.25) | 25-90 | 0.63 |
| **PEP-3 VMI** | 25 | 61.4 (17.38) | 36-100 | 24 | 63.36 (15.02) | 38-93 | 0.53 |
| **VABS-II CS** | 24 | 66.33 (12.07) | 42-88 | 23 | 65.00 (13.8) | 31-92 | 0.63 |
| **VABS-II Communication** | 24 | 64.58 (12.17) | 34-89 | 23 | 58.7 (22.2) | 20-93 | 0.92 |
| **VABS-II Social Skills** | 24 | 63.92 (13.78) | 30-86 | 23 | 68.2 (10.7) | 41-92 | 0.09 |
| **VABS-II Daily Living** | 24 | 63.25 (24.5) | 20-90 | 23 | 71.6 (14.8) | 21-93 | 0.05 |

ADOS-2: Autism Diagnostic Observation Schedule – Second Edition; CS: Composite Score; CVP: Cognitive Verbal-Preverbal; EL: Expressive Language; FM: Fine Motor; GM: Gross Motor; GMDS-ER: Griffith Mental Developmental Scale - Extended Revised; GQ: Global Quotient; PEP: Psychoeducational Profile; RL: Receptive Language; RRB: Repetitive and Restricted Behaviors SA: Social Affect; VABS-II: Vineland Adaptive Behavior Scale – Second Edition; VMI: Visuo-motor Imitation.

**Supplementary Table S2.** CGI-I scores and ESDM response profiles of the 32 children enrolled in this study, followed by the T2 – T0 % difference in GMDS-ER subscales (n = 32) and ADOS-2 Total score (n = 24).

Improvement by > 25% is highlighted in bold and gray.

† GMDS-ER % difference not informative of treatment response, because GQ >70 already at intake.

|  | **CGI-I score** | **ESDM response profile** | **GMDS-ER (% diff)** | **ADOS-2 total score (% diff)** |
| --- | --- | --- | --- | --- |
| **Id. n.** | **Locomotor** | **Personal-Social** | **Language** | **Visuomotor Coordination** | **Performance** | **GQ** |
| 1 | 1 | Full Responder | **118.75** | -9.21 | **90.7** | -13.92 | 21.69 | 24.24 | n.a. |
| 2 | 1 | Full Responder | **44.26** | **41.56** | **61.9** | **61.76** | **59.74** | 52.05† | n.a. |
| 3 | 1 | Full Responder | -10.05 | 3.54 | 17.5 | 6.82 | -6.3 | 0.00† | **-33.33** |
| 4 | 1 | Full Responder | -10.39 | 14.29 | **89.29** | -10.98 | 6.49 | 7.81 | **-57.14** |
| 5 | 2 | Partial Responder | 14.81 | **32** | **53.13** | **61.76** | **158.82** | 62.86 | n.a. |
| 6 | 2 | Partial Responder | -31.45 | 10.58 | **81.55** | -17.5 | -14.38 | -8.16† | -7.69 |
| 7 | 2 | Partial Responder | -13.87 | **33.56** | **87.5** | **32.72** | 6.03 | 17.82† | **-31.25** |
| 8 | 2 | Partial Responder | **113.96** | **141.79** | -21.43 | **170.59** | **150** | **104.76** | **-36.67** |
| 9 | 2 | Partial Responder | 0 | 19.57 | 2.5 | **96.67** | **38.3** | **26.67** | **-40** |
| 10 | 2 | Partial Responder | **58.62** | **110.53** | **64.29** | **37.5** | 17.46 | **52** | **-50** |
| 11 | 2 | Partial Responder | **47.37** | **56** | **87.8** | 10 | 13.64 | **40.74** | **-33.33** |
| 12 | 2 | Partial Responder | **31.03** | 19.67 | 6.85 | 20.29 | -15.12 | 8.7 | -16.67 |
| 13 | 3 | Low Responder | 1.72 | 9.26 | -26.09 | 3.08 | 2.94 | 0 | 0 |
| 14 | 3 | Low Responder | 19.23 | -8.33 | **68.97** | **83.33** | **114.63** | **58.33** | n.a. |
| 15 | 3 | Low Responder | -20.51 | -48.08 | 9.76 | -28.85 | -30.16 | -25.86 | n.a. |
| 16 | 3 | Low Responder | 10.94 | 21.95 | -9.76 | 1.56 | -2.74 | 7.14 | n.a. |
| 17 | 3 | Low Responder | -20.83 | -13.16 | 5.36 | -13.64 | 25 | -4.88† | n.a. |
| 18 | 3 | Low Responder | -13.68 | **34.55** | -60.19 | -13.59 | -- | -20.00† | n.a. |
| 19 | 3 | Low Responder | -71.43 | -68.65 | -75 | -68.63 | -81.52 | -25.81 | 0 |
| 20 | 3 | Low Responder | -8.35 | -8.11 | -14.88 | -14.66 | -26.09 | -14.29† | 25 |
| 21 | 3 | Low Responder | -0.72 | -2.03 | -12.58 | -4.76 | 13.39 | -1.94 | -22.73 |
| 22 | 3 | Low Responder | 9.59 | 11.15 | -3.56 | 9.03 | -12.05 | 5.85 | 72.73 |
| 23 | 3 | Low Responder | **45.44** | 20.62 | **116.67** | **32.95** | 0.14 | **32.6** | 7.14 |
| 24 | 3 | Low Responder | 7.14 | 12.24 | -10.31 | 2.74 | **50** | 12.24 | 25 |
| 25 | 3 | Low Responder | 6.67 | 13.21 | -25.53 | 3.17 | **31.6** | 3.17 | -21.05 |
| 26 | 3 | Low Responder | -6.25 | -24.19 | -39.58 | -3.17 | -29.23 | -25 | 9.52 |
| 27 | 3 | Low Responder | -27.63 | **126.32** | -44.83 | 16.67 | -9.38 | 2.13 | 9.52 |
| 28 | 3 | Low Responder | **27.27** | 6.52 | -17.02 | 0 | 6.82 | 4.35 | -23.81 |
| 29 | 3 | Low Responder | **38.98** | **25.58** | -21.05 | 15.38 | 0 | 14 | 10 |
| 30 | 3 | Low Responder | **28.3** | -6.38 | **26.67** | -11.9 | -2.08 | -16.67 | -19.05 |
| 31 | 3 | Low Responder | -10.87 | -29.63 | -29.27 | -22.03 | -28.99 | -22.68 | -5.26 |
| 32 | 3 | Low Responder | **50** | 5.17 | 0 | -17.57 | 12.35 | 10.58 | -13.04 |
|  |  |  |  |  |  |  |  |  |  |

ADOS-2: Autism Diagnostic Observation Schedule – Second Edition; GMDS-ER: Griffiths Mental Developmental Scale - Extended Revised; GQ: Global Quotient. n.a.: not available.

**Supplementary Table S3.** Estimates, coefficients, statistics and p-values of non-significant Fisher’s Exact Test and logistic regression analyses of all variables assessed as possible predictors of response to ESDM treatment, including pretreatment ADOS-2, ADI-R, GMDS-ER, PEP-3 and VABS-II subscale scores, joint attention, imitation, eye contact, play skills and chronological age (see Methods).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  | ***Overall goodness of fit*** |
|  | ***N*** | ***b*** | **SE B** | ***z*** | ***p*** | **OR (CI)** | ***χ²*** | ***p*** |
| **ADI-R A** | 25 | -0.05 | 0.08 | -0.66 | 0.50 | 0.95 (0.80-1.12) | 0.43 | 0.51 |
| **ADI-R B** | 25 | 0.00 | 0.09 | 0.04 | 0.96 | 1.00 (0.84-1.23) | 0.00 | 0.97 |
| **ADI-R D** | 24 | -0.01 | 0.45 | -0.02 | 0.98 | 0.99 (0.40-2.57) | 4e-04  | 0.98 |
| **ADOS-2 RRB** | 24 | -0.12 | 0.21 | -0.56 | 0.58 | 0.89 (0.55-1.30) | 0.34 | 0.56 |
| **ADOS-2 SA** | 24 | -0.17 | 0.12 | -1.45 | 0.15 | 0.85 (0.66-1.05) | 2.20 | 0.14 |
| **ADOS-2 Total** | 24 | -0.14 | 0.10 | -1.40 | 0.16 | 0.87 (0.70-1.04) | 2.20 | 0.14 |
| **Age at intake** | 32 | 0.08 | 0.09 | 0.98 | 0.33 | 1.08 (0.92-1.30) | 1.00 | 0.32 |
| **Eye Contact†** | 31 | --- | --- | --- | 0.07 | --- | --- | --- |
| **GMDS-ER GQ** | 32 | 0.02 | 0.02 | 0.99 | 0.32 | 1.02 (0.98-1.06) | 0.99 | 0.32 |
| **GMDS-ER Locomotor** | 32 | 0.01 | 0.01 | 0.38 | 0.70 | 1.00(0.97-1.03) | 0.14 | 0.71 |
| **GMDS-ER Language** | 32 | 0.02 | 0.02 | 0.87 | 0.39 | 1.02 (0.98-1.06) | 0.76 | 0.38 |
| **GMDS-ER Visuomotor Coordination** | 32 | 0.01 | 0.02 | 0.70 | 0.48 | 1.01 (0.98-1.05) | 0.50 | 0.48 |
| **GMDS-ER Performance** | 31 | 0.02 | 0.01 | 1.43 | 0.15 | 1.02 (0.99-1.05) | 2.11 | 0.15 |
| **Imitation†** | 29 | --- | --- | --- | 0.12 | --- | --- | --- |
| **PEP-3 Fine Motor** | 25 | 0.04 | 0.03 | 1.45 | 0.15 | 1.04 (0.98-1.09) | 2.22 | 0.13 |
| **PEP-3 Gross Motor** | 25 | 0.02 | 0.02 | 0.96 | 0.34 | 1.02 (0.98-1.07) | 0.92 | 0.34 |
| **Play†** | 31 | --- | --- | --- | 0.15 | --- | --- | --- |
| **VABS-II Daily Living** | 24 | 0.01 | 0.02 | 0.67 | 0.50 | 1.01 (0.98-1.05) | 0.47 | 0.49 |
| **VABS-II Composite Score** | 24 | 0.03 | 0.04 | 0.80 | 0.42 | 1.03 (0.96-1.11) | 0.67 | 0.41 |
| **VABS-II Motor Skills** | 24 | 0.11 | 0.06 | 1.79 | 0.07 | 1.12 (0.99-1.29) | 3.82 | 0.05 |
| **VABS-II Social Skills** | 24 | 0.00 | 0.04 | 0.07 | 0.94 | 1.00 (0.94-1.07) | 0.00 | 0.94 |

**†**Fisher’s exact test.

ADI-R: Autism Diagnostic Interview – Revised; ADOS-2: Autism Diagnostic Observation Schedule – Second Edition; GMDS-ER: Griffith Mental Developmental Scale – Extended Revised; GQ: Global Quotient; PEP: Psychoeducational Profile; RRB: Repetitive and Restricted Behaviors; SA: Social Affect; VABS-II: Vineland Adaptive Behavioral Scales – Second Edition.