Table F-6. Key findings in studies of other medical interventions

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
Donepezil			
Handen et al., 2005[74] RCT G1: Donepezil (2.5-10 mg/day), 18/15 G2: Placebo (NA), 16/16 10 weeks/EOT Moderate RoB	Age, mean (range) G1: 11 yrs 6 mos (8 yrs 7 mos – 16 yrs 8 mos) G2: 11 yrs 8 mos (8 yrs 1 mo – 16 yrs 6 mos) IQ G1: 96.8 (73-142) G2: 96.7 (82-146)	Trail Making Test G1: 123.6 56.5 G2: 154.9 77.8 Verbal Fluency-total number of verbal fluency switches G1: 6.83 3.17 G2: 8.31 2.73 Design Fluency-number of design fluency test switches G1: 3.44 2.5 G2: 4.75 2.79 Color-Word Interference-inhibition/switch time G1: 93.3 38.3 G2: 90.5 25.4 Sorting Test (STCC and STFS)-number of confirmed correct sorts G1: 6.72 2.97 G2: 7.19 1.87 Sorting Test (STCC and STFS)-total number of free sorts G1: 25.2 11.1 G2: 26.6 7.6 Twenty Questions Test-total number of questions asked G1: 24.7 13.7 G2: 18.9 8.9 Tower of California test-total number of moves G1: 12.1 4.1 G2: 12.3 4.9 Word Context Test-total number of points	**EOT** Trail Making Test G1: 118.3 79.1 G2: 104.7 53.4 G1 Vs G2, p= 0.72 Verbal Fluency-total number of verbal fluency switches G1: 6.17 5.12 G2: 6.94 4.97 G1 Vs G2, p=0.372 Design Fluency-number of design fluency test switches G1: 5.22 2.69 G2: 4.31 4.25 G1 Vs G2, p=0.57 Color-Word Interference-inhibition/switch time G1: 81.3 28.9 G2: 79.7 34.2 G1 Vs G2, p=0.74 Sorting Test (STCC and STFS)-number of confirmed correct sorts G1: 5.89 3.1 G2: 5.69 4.36 G1 Vs G2, p=0.89 Sorting Test (STCC and STFS)-total number of free sorts G1: 19.4 11.6 G2: 21.7 10.9 G1 Vs G2, p=0.57 Twenty Questions Test-total number of questions asked G1: 22.2 10.8 G2: 15.1 8.5 G1 Vs G2, p=0.06

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		earned G1: 4.9 4.9 G2: 6.1 3.3 EOWPVT-Expressive Language Scaled Score G1: 104.6 22.4 G2: 108.7 17 Memory Test-Percent Correct G1: 40.7 14.1 G2: 47.1 10.3	Tower of California test-total number of moves G1: 15.2 4.7 G2: 14.9 7.7 G1 Vs G2, p=0.94 Word Context Test-total number of points earned G1: 3 3.2 G2: 3.8 4.9 G1 Vs G2, p=0.43 EOWPVT-Expressive Language Scaled Score G1: 3.8 4.9 G2: 109.7 21 G1 Vs G2, p=0.5 Memory Test-Percent Correct G1: 114.5 16.1 G2: 50.2 11 G1 Vs G2, p=0.28
Anti-epileptics			
Hollander et al., 2010[75] RCT G1: Divalproex sodium (125mg qhs - 500mg bid), 16/16 G2: Placebo (NA), 11/11 12 weeks/EOT Low RoB	Age G1: 9.66 ± 2.64 G2: 8.97 ± 2.8 IQ G1: 52.92 ± 18.5 G2: 76.1 ± 26.45	ABC – Irritability G1: 22 ± 7.81 G2: 20.30 ± 7.36 CGI – Irritability G1: 5.13 ± 0.72 G2: 4.73 ± 0.47 The Overt Aggression Scale-Modified (OAS-M) G1: 6.43 ± 1.41 G2: 5.36 ± 2.2 CYBOCS G1: NR G2: NR VABS G1: 37.13 ± 15.9 G2: 42.4 ± 17.21	**EOT** ABC – Irritability G1: 14.5 ± 6.67 G2: 17.70 ± 7.94 G1 vs G2: p= NR CGI – Irritability Response, n (%) G1: 10 (62,5) G2: 1 (9.1) G1 vs G2, p=0.008 The Overt Aggression Scale-Modified (OAS-M) G1: 5.42 ± 2.17 G2: 6.25 ± 1.28 G1 vs G2: p=ns CYBOCS G1: NR G2: NR G1 vs G2:p=ns

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			VABS G1: NR G2: NR G1 vs G2: p=ns
Bumetanide			
Du et al., 2012[76] RCT G1: Bumetanide + ABA (0.5mg/bid), 32/29 G2: ABA only (30-40mins/day), 28/26 3 months/EOT High RoB (Note: Discussed in section on combined treatments in main report)	Age G1: 4.60 ± 1.90 G2: 4.50 ± 1.67 IQ NR	Autism Behavior Checklist G2: 74.68 ± 4.47 G1: 75.61 ± 11.38 G1 vs G2, p=0.700 CARS G2: 37.28 ± 3.53 G1: 36.39 ± 3.85 G1 vs G2, p=0.362 Clinical Global Impressions (CGI) - Improvement and severity G2: 4.48 ± 0.82 G1: 4.47 ± 1.05 G1 vs G2, p=0.975	**EOT** Autism Behavior Checklist G2: 62.88 ± 4.96 G1: 57.47 ± 7.19 G1 vs G2, p< 0.01 CARS G2: 31.64 ± 1.72 G1: 30.79 ± 2.45 G1 vs G2, p=ns Clinical Global Impressions (CGI) - Improvement and severity G1: G1: 3.17 ± 0.38 G2: 3.40 ± 0.50 G1 vs G2, p< 0.05
Lemonnier et al., 2012[77] RCT G1: Bumetanide (0.5mg/bid), 30/27 G2: Placebo (NA), 30/27 3 months/EOT Moderate RoB	Age, months G1: 82.5 ± 23.2 G2: 85.3 ± 21.3 mos IQ NR	CARS G1: 41.6 ± 3.6 G2: 41.1 ± 4.1 CGI NR ADOS-G NR	CARS **(day 90)** G1: 36 ± 5.7 G2: 39.3 ± 4.9G1 vs G2: p= 0.004 CARS **(day 120)** G1: 38.8 ± 4.7 G2: 40.5 ± 3.8 **EOT** CGI G1: 2.04 ± 0.87 G2: 1.56 ± 0.85 G1 vs G2: p=0.017 Significant amelioration G1: 14 (51.8% G2: 6 (22.2) Small amelioration G1: 7 (25.9) G2: 3 (11.1)

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			No amelioration G1: 6 (22.2) G2: 18 (66.6) ADOS-G, mean change scores G1: +7.8 ± 7.4 G2: +5.3 ± 6.6 G1 vs G2: p=ns
HBOT			
Sampanthavivat et al., 2012[78] RCT G1: HBOT (20, 1 hr sessions/day at 153kPa), 29/29 G2: Sham air (20, 1 hr sessions/day at 116kPa), 29/29 20 days/EOT Moderate RoB	Age G1: 6.10 ± 1.17 G2: 5.67 ± 1.01 IQ NR	ATEC-Parent G1: 68.07 ± 25.43 G2: 64.86 ± 22.80 ATEC-Clinician G1: 60.21 ± 19.92 G2: 60.55 ± 21.36 CGIS-Parent G1: 4.03 ± 1.05 G2: 3.79 ± 0.98 CGIS-Clinician G1: 3.62 ± 0.78 G2: 3.83 ± 0.93	**EOT** ATEC-Parent G1: 58.31 ± 21.94 G2: 55.86 ± 24.93 G1 vs G2: p=ns ATEC-Clinician G1: 52.38 ± 19.11 G2: 52.93 ± 18.93 G1 vs G2: p=ns CGIS-Parent G1: 3.69 ± 0.93 G2: 3.66 ± 0.86 G1, p=0.005 G2, p=NS CGIS-Clinician G1: 3.48 ± 0.78 G2: 3.76 ± 0.83 G1 vs G2: p=ns Change scores CGIC-Parent G1: 2.34 ± 0.61 G2: 2.55 ± 0.83 G1 vs. G2:p=ns CGIC-Clinician G1: 2.31 ± 0.6 G2: 2.72 ± 0.8 G1 vs G2:, p=0.03
Granpeesheh et al., 2010[79] RCT G1: HBOT (24% oxygen at 1.3 atm pressure), 18/17 G2: Placebo (NA), 16/16 15 weeks/EOT	Age G1: 6.11 G2: 6.25 IQ NR	SRS NR ADOS NR	**Mean change score:** SRS- Social Awareness G1: -3.14 ± 14.21 G2: -1.33 ± 16.62 G1 vs G2: p=ns SRS-Social Cognition

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
Low RoB			G1: 1.79 ± 8.82 G2: -5.33 ± 16.01 G1 vs G2: p=ns SRS-Social Communication G1: -1.00 ± 13.06 G2: 3.13 ± 12.02 G1 vs G2:p=ns SRS-Social Motivation G1: -5.50 ± 12.45 G2: -6.33 ± 13.12 G1 vs G2:p=ns SRS-Autistic Mannerisms G1: 1.64 ± 14.58 G2: -3.33 ± 12.49 G1 vs G2, p=0.33 Number (%) improving ADOS-Total G1: 5/18 (27.8) G2: 4/16 (25) G1 vs G2: p=ns ADOS-Communication G1: 3/18 (16.7) G2: 2/16 (12.5) G1 vs G2: p=ns ADOS-Socialization G1: 3/18 (16.7) G2: 2/16 (12.5) G1 vs G2: p=ns
Rossignol 2009[80] RCT G1: HBOT (1.3 atm and 24% oxygen), 33/30 G2: Room air (1.03 atm and 21% oxygen), 29/26 4 weeks/EOT Low RoB	Age G1: 4.97 ± 1.29 G2: 4.86 ± 1.13 IQ NR	ABC – Irritability G1: 13.2 ± 9.5 G2: 12.2 ± 7.9 ABC – Social Withdrawal/Lethargy G1: 10.5 ± 6.9 G2: 11.2 ± 6.9 ABC – Stereotypic Behavior G1: 7.5 ± 4.9 G2: 6.2 ± 4.7	ABC – Irritability G1: 10.5 ± 7.4 G2: 11.3 ± 6.4 G1 vs G2: p=0.0976 ABC – Social Withdrawal/Lethargy G1: 9.3 ± 6.7 G2: 8.9 ± 5.6 G1 vs G2: p=ns ABC – Stereotypic Behavior

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post- treatment scores, mean ± SD
		ABC – Hyperactivity G1: 20.7 ± 9.9 G2: 20.1 ± 8.2 ABC – Inappropriate Speech G1: 3.4 ± 3.1 G2: 3.6 ± 3.6 ATEC – Total Score G1: 75.3 ± 19.5 G2: 75.6 ± 21	G1: 6.2 ± 5.1 G2: 5.4 ± 4 G1 vs G2: p=ns ABC – Hyperactivity G1: 17.8 ± 9.2 G2: 16.8 ± 7.7 G1 vs G2: p=ns ABC – Inappropriate Speech G1: 2.6 ± 2.5 G2: 3.3 ± 3.2 ATEC – Total Score G1: 65.9 ± 16.4 G2: 70.1 ± 21.9 G1 vs G2: p=ns CGI – Improvement (Much or very much improved) G1: 9 (30) G2: 2 (7.7) G1 vs G2: p=0.0471
Melatonin			
Cortesi et al., 2012[81] RCT G1: Controlled-release melatonin + CBT (3mg/day), 40/35 G2: Controlled-release melatonin (3mg/day), 40/34 G3: CBT (4 sessions/week), 40/33 G4: Placebo (NA), 40/32 12 weeks/EOT Low (Note: Discussed in section on combined treatments in main report)	Age G1: 6.4 ± 1.1 G2: 6.8 ± 0.9 G3: 7.1 ± 0.7 G4: 6.3 ± 1.2 IQ NR	CSHQ CSHQ-Total score G1: 66.11 ± 5.47 G2: 66.67 ± 8.55 G3: 64.48 ± 5.48 G4: 64.20 ± 4.85 Bed resistance G1: 14.53 ± 1.82 G2: 13.85 ± 2.23 G3: 13.44 ± 2.08 G4: 13.63 ± 1.82 SOD G1: 2.88 ± 0.32 G2: 2.85 ± 0.35 G3: 2.89 ± 0.30 G4: 2.90 ± 0.31 Sleep anxiety G1: 7.95 ± 1.83 G2: 8.35 ± 2.19	**EOT** CSHQ CSHQ-Total score G1: 47.84 ± 2.94 G2: 54.78 ± 6.22 G3: 60.06 ± 4.71 G4: 64.80 ± 4.52 Time x group p<0.001 Bed resistance G1: 8.46 ± 1.39 G2: 10.50 ± 2.20 G3: 11.62 ± 2.22 G4: 14.10 ± 1.93 Time x group p<0.001 SOD G1: 1.69 ± 0.73 G2: 2.10 ± 0.68 G3: 2.51 ± 0.57 G4: 2.93 ± 0.25 Time x group p<0.001

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		G3: 8.62 ± 1.98 G4: 7.66 ± 1.73 Night-wakings G1: 7.61 ± 0.89 G2: 7.67 ± 0.94 G3: 7.62 ± 0.94 G4: 7.76 ± 0.93 Sleep duration G1: 7.34 ± 1.35 G2: 7.17 ± 1.51 G3: 7.01 ± 1.48 G4: 6.46 ± 1.25 Parasomnias G1: 9.15 ± 1.68 G2: 9.10 ± 2.42 G3: 9.75 ± 2.11 G4: 8.96 ± 1.80 SDB G1: 3.18 ± 0.40 G2: 3.20 ± 0.44 G3: 3.10 ± 0.30 G4: 3.15 ± 0.40 DS G1: 13.92 ± 2.86 G2: 13.35 ± 3.84 G3: 13.31 ± 2.67 G4: 13.13 ± 3.11 Sleep Diary TST G1: 414.03 ± 45.34 G2: 410.28 ± 45.07 G3: 408.08 ± 49.03 G4: 413.00 ± 45.13 SOL G1: 85.84 ± 20.02 G2: 81.21 ± 32.35 G3: 76.34 ± 31.70 G4: 78.20 ± 33.83 WASO G1: 69.50 ± 23.35 G2: 73.71 ± 45.00 G3: 68.72 ± 31.77 G4: 69.75 ± 45.21	Sleep anxiety G1: 5.23 ± 0.95 G2: 7.21 ± 1.87 G3: 7.17 ± 1.48 G4: 7.93 ± 1.99 Time x group p<0.001 Night-wakings G1: 4.42 ± 0.90 G2: 5.03 ± 1.10 G3: 7.06 ± 1.06 G4: 7.86 ± 0.81 Time x group p<0.001 Sleep duration G1: 4.38 ± 1.02 G2: 4.82 ± 0.94 G3: 6.68 ± 1.16 G4: 6.40 ± 1.29 Time x group p<0.001 Parasomnias G1: 8.92 ± 1.38 G2: 9.35 ± 1.78 G3: 9.82 ± 2.25 G4: 9.16 ± 1.53 Time x group p=ns SDB G1: 3.22 ± 0.35 G2: 3.15 ± 0.48 G3: 3.20 ± 0.41 G4: 3.20 ± 0.44 Time x group p=ns DS G1: 10.84 ± 1.68 G2: 11.39 ± 2.34 G3: 11.96 ± 1.97 G4: 12.96 ± 1.97 Time x group p<0.001 Sleep Diary TST G1: 505.01 ± 31.18 G2: 481.10 ± 33.15 G3: 445.13 ± 48.37 G4: 416.23 ± 43.60 Time x group p<0.001

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		NAPTIME G1: 28.26 ± 49.13 G2: 33.57 ± 56.63 G3: 35.31 ± 60.17 G4: 37.33 ± 56.19 SE G1: 70.26 ± 4.83 G2: 71.10 ± 4.91 G3: 71.37 ± 4.77 G4: 71.13 ± 4.99 BEDTIME G1: 23.33 ± 1.35 G2: 23.45 ± 1.15 G3: 23.39 ± 1.03 G4: 23.41 ± 1.19	SOL G1: 33.69 ± 14.40 G2: 45.21 ± 23.21 G3: 59.13 ± 27.60 G4: 79.60 ± 31.85 Time x group p<0.001 WASO G1: 29.69 ± 12.97 G2: 42.21 ± 22.35 G3: 61.17 ± 28.93 G4: 70.15 ± 42.76 Time x group p<0.001 NAPTIME G1: 9.20 ± 22.48 G2: 17.00 ± 33.11 G3: 12.29 ± 24.24 G4: 36.10 ± 33.28 Time x group p=ns SE G1: 84.46 ± 4.23 G2: 82.71 ± 4.00 G3: 79.58 ± 2.82 G4: 71.93 ± 4.62 Time x group p<0.001 BEDTIME G1: 22.06 ± 1.05 G2: 22.30 ± 1.10 G3: 22.55 ± 1.01 G4: 23.51 ± 1.12 Time x group p<0.001
Wright et al., 2011[82] RCT G1: Melatonin (2-10mg/day), 9/6 G2: Placebo (NA), 11/10 Crossover 9 months/EOT Moderate RoB	Age G1: 8.9 ± 3.0 G2: 8.5 ± 2.3 IQ NR	Dysomnias, n=12 G1+G2: 34.0 ± 9.4 Parasomnias, n=14 G1+G2: 18.7 ± 7.7 Sleep apneas, n=13 G1+G2: 13.0 ± 9.4 Other sleep disorders, n=10 G1+G2: 25.1 ± 5.6 DBC-Total, n=17 G1+G2: 90.1 ± 18.7	**EOT** Dysomnias, n=12 G1: 22.2 ± 6.6 G2: 27.8 ± 6.3 p=0.04 Parasomnias, n=14 G1: 17.3 ± 4.5 G2: 20.1 ± 8.1 p=ns Sleep apneas, n=13 G1: 11.4 ± 4.2 G2: 12.7 ± 3.4 p=ns

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		DBC-Disruptive, n=17 G1+G2: 26.2 ± 13.0 DBC- Self-absorption, n=17 G1+G2: 33.0 ± 11.0 DBC-Communication, n=17 G1+G2: 11.4 ± 3.6 DBC-Anxiety, n=17 G1+G2: 8.8 ± 2.8 DBC-Social relating, n=17 G1+G2: 9.4 ± 3.1 GHQ total n=17 G1+G2: 3.7 ± 7.1 No. of wakenings n=17 G1+G2: 0.5 ± 0.5 Total sleep minutes, n=17 G1+G2: 499.9 ± 66.4 Sleep latency, n=17 G1+G2: 135.0 ± 63.0	Other sleep disorders, n=10 G1: 23.8 ± 3.4 G2: 25.9 ± 6.2 p=ns DBC-Total G1: 75.12 ± 23.29 G2: 82.25 ± 25.79 p=0.05 DBC-Disruptive G1: 21.82 ± 11.97 G2: 23.88 ± 11.12 p=ns DBC- Self-absorption G1: 28.94 ± 13.41 G2: 30.06 ± 14.05 p=ns DBC-Communication G1: 8.24 ± 3.29 G2: 9.75 ± 5.04 p=0.045 DBC-Anxiety G1: 7.53 ± 3.39 G2: 7.56 ± 3.86 p=ns DBC-Social relating G1: 7.82 ± 3.11 G2: 9.06 ± 4.27 p=ns GHQ total G1: 1.4 ± 2.7 G2: 3.2 ± 4.6 p=ns No. of wakenings G1: 0.43 ± 0.64 G2: 0.58 ± 0.74 p=ns Total sleep minutes G1: 556.11 ± 53.59 G2: 507.66 ± 70.67 p=0.002

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			Sleep latency G1: 82.84 ± 50.61 G2: 124.79 ± NR p=0.004
Other			
Amatachaya et al., 2014[83, 84] RCT G1: Transcranial direct current stimulation (1mA), 10/10 G2: Sham (NA), 10/10 8 weeks/EOT Moderate RoB	Age G1 + G2: 5-8 IQ NR	CARS G1: 34.95 ± 4.73 G2: 34.6 ± 4.41 ATEC-Total G1: 67.25 ± 9.88 G2: 69.15 ± 8.98 ATEC-Language G1: 10.6 ± 5.59 G2: 10.75 ± 4.72 ATEC- Social G1: 16.4 ± 4.5 G2: 17.45 ± 2.67 ATEC-Sensory and cognitive awareness G1: 20.1 ± 3.91 G2: 20.5 ± 3.4 ATEC-Health and behavioral problem G1: 20.15 ± 8.34 G2: 20.45 ± 7.21 CGAS G1: 54.35 ± 11.07 G2: 53.35 ± 10.31 CGI-Severity G1: 4.05 ± 0.94 G2: 4.15 ± 0.99	**EOT** CARS G1: 32.2 ± 3.98 G2: 35 ± 4.3 p < 0.05 ATEC-Total G1: 58 ± 5.28 G2: 69.65 ± 9.13 p ≤ 0.001 ATEC-Language G1: 10.5 ± 5.39 G2: 10.55 ± 5.2 ATEC- Social G1: 14.45 ± 4.85 G2: 17.7 ± 2.98 p < 0.05 ATEC-Sensory and cognitive awareness G1: 18.35 ± 5.35 G2: 22.3 ± 4.47 p < 0.05 ATEC-Health and behavioral problem G1: 14.7 ± 6.21 G2: 19.1 ± 6.47 p < 0.05 CGAS G1: 60 ± 10.57 G2: 53.1 ± 10.14 p < 0.05 CGI-Improvement, n (%) Very much improved G1: 0 G2: 0 p=ns

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post- treatment scores, mean ± SD
			Much improved G1: 9 (45) G2: 3 (15) p≤ 0.05 Minimally improved G1: 8 (40) p=ns No change G1: 1 (5) G2: 6 (30) p=ns Minimally worse G1: 2 (10) G2: 2 (10) p=ns Much worse G1: 0 G2: 5 (25) p < 0.05 Very much worse G1: 0 G2: 0 p=ns
Dadds et al., 2014[85] RCT G1: Intranasal oxytocin (12 or 24 IU), 19/19 G2: Placebo (NA), 19/189 4 days/EOT Moderate RoB	Age G1: 11.79 ± 2.82 G2: 10.74 ± 2.38 IQ G1: 90.47 ± 11.70 G2: 88.64 ± 7.98	SRS G1: 17.13 ± 5.57 G2: 20.56 ± 6.70 Video Observation Repetitive Behaviors G1: 0.24 ± 0.26 G2: 0.20 ± 0.25 Video Observation Social Interaction Skills G1: 1.63 ± 0.50 G2: 1.69 ± 0.38 Facial Emotion Recognition G1: 0.79 ± 0.11 G2: 0.77 ± 0.14 OSU G1: 3.76 ± 0.70 G2: 4.17 ± 0.79	3 mos follow-up SRS G1:16.47 ± 5.94 G2: 15.78 ± 7.85 G1 vs G2: p=ns Video Observation Repetitive Behaviors G1: 0.27 ± 0.24 G2: 0.25 ± 0.24 G1 vs G2: p=ns Video Observation Social Interaction Skills G1: 1.92 ± 0.51 G2: 1.96 ± 0.49 G1 vs G2: p=ns Facial Emotion Recognition G1: 0.87 ± 0.08 G2: 0.86 ± 0.07 G1 vs G2: p=ns

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post- treatment scores, mean ± SD
		CARS G1: 32.26 ± 3.25 G2: 33.84 ± 3.70	OSU G1: 3.60 ± 0.63 G2: 3.78 ± 0.94 G1 vs G2: p=ns CARS G1: 30.07 ± 2.78 G2: 31.06 ± 5.20 G1 vs G2: p=ns
Klaiman et al., 2013[86] RCT G1: Tetrahydrobiopterin (20mg/kg/day), 23/23 G2: Placebo (NA), 23/23 16 weeks/EOT Low RoB	Age, months G1: 60.1 ± 12.0 G2: 60.2 ± 12.6 IQ NR	CGI-Severity [N (%)] Frequency of markedly, severely, or extremely ill G1: 10 (48) G2: 15 (68) ABC-Irritability G1: 11.1 ± 7.7 G2: 11.9 ± 7.8 ABC-Social withdrawal/lethargy G1: 9.5 ± 7.5 G2: 16.2 ± 10.0 ABC-Stereotypy G1: 6.1 ± 3.9 G2: 6.1 ± 3.6 ABC-Hyperactivity G1: 21.5 ± 10.3 G2: 22.9 ± 11.6 ABC-Inappropriate speech G1: 3.7 ± 2.4 G2: 3.4 ± 4.1 SRS G1: 81.4 ± 10.3 G2: 83.6 ± 9.2 PLS G1: 77.8 ± 29.2 G2: 57.1 ± 25.7 Vineland G1: 320.5 ± 47.9 G2: 274.4 ± 51.4	16 wks follow-up CGI-Severity, N (%) Frequency of markedly, severely, or extremely ill G1: 7 (35) G2: 14 (64) G1 vs G2: p=ns Improvement, frequency of very much or much improved G1: 5 (25) G2: 3 (14) G1 vs G2: p=ns ABC-Irritability G1: 10.0 ± 7.8 G2: 10.8 ± 7.8 G1 vs G2: p=ns ABC-Social withdrawal/lethargy G1: 5.2 ± 4.4 G2: 13.6 ± 7.5 G1 vs G2: p<0.01 ABC-Stereotypy G1: 5.4 ± 3.8 G2: 6.7 ± 4.5 G1 vs G2: p=ns ABC-Hyperactivity G1: 18.2 ± 8.5 G2: 22.8 ± 10.3 G1 vs G2: p=ns ABC-Inappropriate speech G1: 2.6 ± 1.9

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			G2: 3.9 ± 3.6 G1 vs G2: p=ns SRS G1: 76.7 ± 10.9 G2: 83.2 ± 10.4 G1 vs G2: p=ns PLS G1: 84.0 ± 28.8 G2: 60.4 ± 25.4 G1 vs G2: p=0.01 Vineland G1: 344.76 ± 50.0 G2: 294.9 ± 70.1 G1 vs G2: p=0.02
Lv et al., 2013[87] NRCT G1: Human cord blood mononuclear cells (CBMNCs) (2 × 10^6/kg) + rehabilitation therapy, 14/14 G2: CBMNCs + umbilical cord-derived mesenchymal stem cells (UCMSCs) (2 x 10^6/kg and 1 × 10^6/kg) + rehabilitation, 9/9 G3: Rehabilitation therapy, 14/13 5-7 days (4 transplants)/EOT High RoB	Age G1: 7.41 ± 2.63 G2: 6.20 ± 2.12 G3: 5.60 ± 2.01 IQ G1: NR G2: NR G3: NR	CARS G1: 46.43 ± 8.65 G2: 45.11 ± 4.31 G3: 43.15 ± 4.38 CGI NR ABC-Total G1: 94.07 ± 21.98 G2: 91.78 ± 25.92 G3: 75.46 ± 12.05 ABC-Irritability G1: 16.36 ± 9.61 G2: 15.00 ± 7.81 G3: 9.15 ± 5.58 ABC-Lethargy/Social withdrawal G1: 30.71 ± 6.08 G2: 31.00 ± 6.98 G3: 35.08 ± 4.96 ABC-Stereotypic behavior G1: 29.43 ± 9.77 G2: 28.33 ± 8.47 G3: 22.77 ± 6.86 ABC-Hyperactivity G1: 11.86 ± 4.55 G2: 11.89 ± 6.88 G3: 6.08 ± 3.15	**EOT** CARS G1: 37.14 ± 10.15 G2: 28.00 ± 6.18 G3: 37.23 ± 3.42 CGI-GI [N (%)] Very much improved G1: 1 (7.14) G2: 3 (33.33) G3: 0 (0) Much improved G1: 6 (42.86) G2: 5 (55.56) G3: 1 (7.69) Minimally improved G1: 2 (14.29) G2: 1 (11.11) G3: 11 (84.62) No change G1: 5 (35.71) G2: 0 (0.00) G3: 1 (7.69) Minimally worse G1: 0 (0.00) G2: 0 (0.00) G3: 0 (0.00) Much worse G1: 0 (0.00)

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post- treatment scores, mean ± SD
		ABC-Inappropriate speech G1: 5.71 ± 4.30 G2: 5.56 ± 2.83 G3: 2.38 ± 2.10	G2: 0 (0.00) G3: 0 (0.00) Very much worse G1: 0 (0.00) G2: 0 (0.00) G3: 0 (0.00) CGI-EI [N (%)] Unchanged or worse G1: 5 (35.71) G2: 0 (0.00) G3: 1 (7.69) Minimal G1: 2 (14.29) G2: 1 (11.11) G3: 11 (84.62) Moderate G1: 7 (50.00) G2: 6 (66.67) G3: 1 (7.69) Marked G1: 0 (0.00) G2: 2 (22.22) G3: 0 (0.00) ABC-Total G1: 58.36 ± 31.73 G2: 36.78 ± 16.95 G3: 62.31 ± 11.3 G1 vs G3+ p<0.05 G2 vs G3: p< 0.05 ABC-Irritability G1: 8.14 ± 8.37 G2: 4.22 ± 3.19 G3: 6.92 ± 4.96 p=ns ABC-Lethargy/Social withdrawal G1: 24.14 ± 9.65 G2: 16.00 ± 7.92 G3: 30.54 ± 5.03 G1 vs G3: p<0.05 G2 vs G3: p<0.05 ABC-Stereotypic

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			behavior G1: 17.07 ± 9.93 G2: 9.33 ± 5.81 G3: 17.31 ± 4.05 G2 vs G3: p,0.05 ABC-Hyperactivity G1: 6.86 ± 5.26 G2: 4.67 ± 3.74 G3: 5.08 ± 2.40 p=ns ABC-Inappropriate speech G1: 2.14 ± 2.32 G2: 2.56 ± 2.19 G3: 2.46 ± 2.63 p=ns
Arnold et al., 2012[88] RCT G1: Mecamylamine (0.5-5 mg/kg/day), 12/10 G2: Placebo (NA), 8/8 14 weeks/EOT Low RoB	Age G1: 6.76 ± 2.24 G2: 8.36 ± 2.83 IQ G1: 77.58 ± 21.12 G2: 62.62 ± 32.53	OACIS-S G1: 5.25 ± 0.75 G2: 5.63 ± 0.74 OARS G1: 1.83 ± 0.42 G2: 2.06 ± 0.45 ABC-Irritability G1: 12.75 ± 9.42 G2: 12.88 ± 9.60 ABC-Lethargy G1: 10.42 ± 6.61 G2: 17.00 ± 9.37 ABC-Stereotype G1: 4.17 ± 3.54 G2: 9.75 ± 6.25 ABC-Hyperactivity G1: 21.08 ± 11.74 G2: 19.13 ± 13.02 ABC-Inappropriate Speech G1: 4.50 ± 3.73 G2: 4.38 ± 3.16 RBS-Stereotypy G1: 4.58 ± 2.87 G2: 7.38 ± 3.16	**Mean change score** OACIS-S G1: -0.58 ± 0.79 G2: -0.63 ± 0.74 OARS G1: -0.30 ± 0.33 G2: -0.32 ± 0.34 ABC-Irritability G1: -3.17 ± 8.76 G2: -5.00 ± 10.78 ABC-Lethargy G1: -4.25 ± 6.97 G2: -7.50 ± 9.56 ABC-Stereotype G1: -1.42 ± 2.64 G2: -1.63 ± 7.11 ABC-Hyperactivity G1: -6.92 ± 11.25 G2: -5.50 ± 12.06 ABC-Inappropriate speech G1: -1.50 ± 3.90 G2: -1.75 ± 2.38 RBS-Stereotypy G1: -1.92 ± 2.94 G2: -0.63 ± 6.21

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		RBS-Self Injury G1: 1.75 ± 2.01 G2: 4.50 ± 3.82 RBS-Compulsive G1: 5.50 ± 3.90 G2: 7.25 ± 4.53 RBS-Ritualistic G1: 6.00 ± 4.63 G2: 5.88 ± 4.91 RBS-Sameness G1: 8.08 ± 5.62 G2: 9.38 ± 6.14 RBS-Restricted G1: 3.92 ± 3.23 G2: 4.13 ± 2.75 SRS-Receptive G1: 11.92 ± 2.64 G2: 16.38 ± 2.62 SRS-Cognitive G1: 19.50 ± 2.88 G2: 22.75 ± 6.04 SRS-Expressive G1: 34.33 ± 8.14 G2: 39.88 ± 11.68 SRS-Motivation G1: 13.00 ± 4.69 G2: 19.13 ± 4.26 SRS-Preoccupations G1: 16.33 ± 6.88 G2: 22.50 ± 7.67 EVT G1: 74.0 ± 16.34 G2: 47.5 ± 24.74	RBS-Self injury G1: -0.83 ± 1.53 G2: -2.88 ± 4.39 RBS-Compulsive G1: -2.42 ± 3.55 G2: -3.50 ± 3.38 RBS-Ritualistic G1: -1.75 ± 4.58 G2: -2.00 ± 3.02 RBS-Sameness G1: -4.67 ± 6.05 G2: -2.50 ± 3.21 RBS-Restricted G1: -1.58 ± 2.50 G2: -1.13 ± 2.64 SRS-Receptive G1: 0.33 ± 1.78 G2: -2.25 ± 3.06 SRS-Cognitive G1: -2.50 ± 5.39 G2: -2.13 ± 5.74 SRS-Expressive G1: -4.17 ± 7.31 G2: -7.25 ± 8.55 SRS-Motivation G1: -3.83 ± 4.55 G2: -5.75 ± 4.89 SRS-Preoccupations G1: -3.33 ± 7.43 G2: -5.75 ± 4.89 EVT G1: -2.14 ± 10.12 G2: 0 ± 6.42
Hardan et al., 2012[89] RCT G1: N-acetylcysteine (NAC) (900 mg up to 3 times/day), 15/134 G2: Placebo, 18/15	Age G1: 7.0 ± 2.1 G2: 7.2 ± 2.2 IQ NR	ABC Irritability G1: 16.9±7.9 G2: 14.8±9.6 ABC Lethargy G1: 15.2±9.5 G2: 12.1±7.8	**EOT** ABC Irritability G1: 7.2±5.7 G2: 13.1±9.9 p<.001 ABC Lethargy

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
12 weeks/EOT Low RoB		ABC Stereotypy G1: 9.1±5.5 G2: 8.9±6.5 ABC Hyperactivity G1: 23.4±9.0 G2: 23.8±9.3 ABC Inappropriate Speech G1: 4.9±3.2 G2: 4.1±3.7 RBS-R Stereotypies G1: 6.7±3.8 G2: 8.1±5.3 RBS Self-Injurious Behavior G1: 3.9±4.4 G2: 3.4±3.8 RBS Compulsions G1: 4.7±3.7 G2: 5.8±4.8 RBS Rituals G1: 5.3±3.7 G2: 6.6±4.5 RBS Sameness G1: 7.8±7.2 G2: 9.2±8.1 RBS Restricted G1: 4.7±3.4 G2: 5.2±3.7 SRS Total G1: 111.9±28.3 G2: 104.7±28.1 SRS Social Awareness G1: 12.7±3.4 G2: 13.5±3.7 SRS Social Cognition G1: 21.9±6.3 G2: 21.2±5.8	G1: 11±9.4 G2: 8.3±7.7 p=.ns ABC Stereotypy G1: 5.6±5.7 G2: 8.0±7.0 p=ns ABC Hyperactivity G1: 12.4±11.4 G2: 21.0±11.5 p=ns ABC Inappropriate Speech G1: 2.5±2.6 G2: 3.6±3.6 p=ns RBS Stereotypies G1: 4.6±3.4 G2: 6.9±5.2 p= .014 RBS Self Injurious Behavior G1: 2.2±2.3 G2: 3.0±3.6 p=ns RBS Compulsions G1: 2.5±2.1 G2: 5.2±5.0 p=ns RBS Rituals G1: 4.3±3.4 G2: 5.6±4.9 p=ns RBS Sameness G1: 5.3±4.7 G2: 7.9±6.2 p=ns RBS Restricted G1: 3.5±2.3 G2: 4.8±3.6 p=ns

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		SRS Social Communication G1: 39.6±11.3 G2: 39.3±8.6 SRS Social Motivation G1: 16.6±6.3 G2: 16.9±6.5 SRS Autism Mannerisms G1: 21.7±5.6 G2: 21.4±7.3 CGI Severity G1: 5.1±0.7 G2: 5.3±0.8	SRS Total G1: 93.8±26.7 G2: 98.5±37.8 p=ns SRS Social Awareness G1:11.5±3.3 G2: 13.4±4.7 p=ns SRS social Cognition G1: 18.8±7.0 G2: 18.9±5.6 p=.037 SRS Social Communication G1: 33.3±10.9 G2: 34.5±14.5 p=.ns SRS Social Motivation G1: 13.0±4.7 G2: 14.5±7.0 p=ns SRS Autism Mannerisms G1: 16.0±6.1 G2: 20.3±6.9 p=.045 CGI Severity G1: 4.5±0.8 G2: 4.9±0.9 p=ns CGI Improvement G1: 2.9±1.1 G2: 3.2±.09 p=ns
Chez et al., 2003[90] RCT G1: Donepezil hydrochloride only, / G2: Placebo/ Donepezil hydrochloride, / 12 wks/EOT Moderate RoB	Age G1: 6.8 (2.1-9.9) G2: 6.9 (4.1-10.3) IQ NR	CARS G1: 34.7 ± 7.7 G2: 35.1 ± 7.9 Expressive One-Word Picture Vocabulary Test (speech age in months) G1: 35.7 ± 27.8 G2: 31.9 ± 31.1	End of 6 wks CARS G1: 33.3 ± 8 G2: 32.9 ± 7.7 Expressive One-Word Picture Vocabulary Test (speech age in months) G1: 43.3 ± 27.2

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		Receptive One-Word Picture Vocabulary Test (speech age in months) G1: 38.8 ± 23.5 G2: 33.5 ± 27.9	G2: 33.8 ± 32.9 Receptive One-Word Picture Vocabulary Test (speech age in months) G1: 50.3 ± 27 G2: 39.83 ± 27 **EOT** CARS G1: 30.8 ± 7.9 G2: 30.9 ± 9.1 G1 vs G2, p<0.05 Expressive One-Word Picture Vocabulary Test (speech age in months) G1: 42.5 ± 28.5 G2: 40.9 ± 38.8 G1 vs G2, p<0.05 Receptive One-Word Picture Vocabulary Test (speech age in months) G1: 49.7 ± 34.2 G2: 87.37 ± 14.2 G1 vs G2, p<0.05
King et al., 2001[91] RCT G1: Amantadine, 19/17 G2: Placebo, 20/17 4 wks/EOT Moderate RoB	Age 5-19 IQ >35	ABC – Irritability G1: 19.1 (3-38) G2: 18.7 (3-33) ABC – Hyperactivity G1: 29.4 (16-42) G2: 32.7 (17-46) CGI – Severity (Mild) G1: 0 (0) G2: 1 (5) CGI – Severity (Moderate) G1: 11 (57.8) G2: 11 (55) CGI – Severity (Severe) G1: 8 (42.1) G2: 7 (35)	**EOT** ABC – Response rate (Reduction of at least 25% for irritability and/or hyperactivity) G1: 7 (37) G2: 9 (47) G1 vs G2, p=ns CGI – Improvement (Marked Improvement) G1: 5 (26) G2: 1 (5)

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
Duffy et al., 2014[92] Retrospective Cohort G1: Steroid (2 mg/kg/day), 20/20 G2: Control (non- steroid treated) (NA), 24/24 4-14 months/EOT High RoB	Age G1: 3.909 ± 1.248 G2: 4.522 ± 1.800 IQ G1: NR G2: NR	EEG NR FMAER NR	**Mean change score** EEG change, n Improved G1: 3 G2: 8 No change G1: 10 G2: 12 Worse G1: 7 G2: 4 G1 vs G2: p=ns CLSQ mean change in scores Receptive G1: 4.80 G2: 0.167 Expressive G1: 4.10 G2: 0.542 Change in language scores, n Receptive Better G1: 17 G2: 6 No difference G1: 3 G2: 16 Worse G1: 0 G2: 2 G1 vs G2: p≤0.0002 Expressive Better G1: 17 G2: 10 No difference G1: 2 G2: 13 Worse

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			G1: 1 G2: 1 G1 vs G2: p≤0.0031
Wasserman et al., 2006[93] RCT G1: Levetiracetam (862.50 ± 279.19 mg/day), 10/9 G2: Placebo (ND), 10/8 10 weeks/EOT Low ROB	Age G1: 7.62 ± 1.69 G2: 9.82 ± 3.95 IQ-Leiter-R G1: 38 ± 28.7 G2: 60.43 ± 26.4 IQ-WISC G1: 91.33 ± 14.6 G2: 29 ± 0	CGI-Autistic Disorder Severity G1: 4.2 ± 0.79 G2: 4.3 ± 1.16 CYBOCS-Compulsion G1: 14.3 ± 2.62 G2: 14.8 ± 3.8	CYBOCS-Compulsion G1 vs G2, p=0.013 **Parent** ABC-Irritability G1 vs G2, p=ns ABC-Social Withdrawal/Lethargy G1 vs G2, p=ns, z=-1.786, SE=0.133 ABC-Stereotypic Behavior G1 vs G2, p=ns, z=-0.042, SE=0.102 ABC-Hyperactivity G1 vs G2, p=ns, z=-0.462, SE=0.091 ABC-Inappropriate Speech G1 vs G2, p=ns, z=0.099, SE=0.099 **Teacher** ABC-Irritability G1 vs G2, p=0.003, z=-2.955, SE=0.109 ABC-Social Withdrawal/Lethargy G1 vs G2, p=ns, z=-0.623, SE=0.166 ABC-Stereotypic Behavior G1 vs G2, p=ns, z=0.401, SE=0.127 ABC-Hyperactivity G1 vs G2, p=ns, z=-0.653, SE=0.094 ABC-Inappropriate Speech G1 vs G2, p=ns, z=-

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			0.268, SE=0.105
Danfors et al., 2005[94] RCT G1: Tetrahydrobiopterin/Placebo (3mg/kg),12 G2: Placebo/ Tetrahydrobiopterin (ND), 12 12 months/EOT Moderate ROB	Age 4-7 IQ NR	CARS-Total Score G1: 35.4 ± 2.6 G2: 37.4 ± 7.1 Social Interaction G1: 9 ± 0.6 G2: 10.8 ± 1.6	Points Decreased CARS-Total Score G1: 2.1 ± 2.1 G2: 2.1 ± 4.3 G1 vs G2, p=ns Social Interaction G1: 1.6 ± 1.1 G2: 0.3 ± 1.4 G1 vs G2, p=0.04
Dean et al., 2016[95] RCT G1: N-acetyl cysteine (500 mg/day), 48/34 G2: Placebo (ND),50 /37 6 months/EOT Moderate ROB	Age G1: 78.4 ± 21.7 G2: 74.9 ± 23.8 IQ G1: 74.3 ± 15.6 G2: 71.7 ± 13.8	SRS-Total Score G1: 102.9 ± 26.4 G2: 99.7 ± 24.8 CCC-General Communication G1: 33.6 ± 13.1 G2: 34.7 ± 14.6 CCC-Social Interaction Deviance G1: 3.1 ± 8.5 G2: 3.3 ± 6.7 Repetitive Behavior Scale-Total Score G1: 28.5 ± 19.4 G2: 24.8 ± 14.1 CGI-Severity G1: 4.1 ± 1 G2: 4.2 ± 1 Developmental Behavior Checklist-Total Score G1: 57 ± 23.2 G2: 59 ± 27.6	SRS-Total Score G1: 92.1 ± 29.3 G2: 88.7 ± 27.7 G1 vs G2, p=ns CCC-General Communication G1: 34.7 ± 11.9 G2: 41.5 ± 16.5 G1 vs G2, p=ns CCC-Social Interaction Deviance Change Score G1: 0.05 ± 8.4 G2: -2.2 ± 8.2 G1 vs G2, p=ns Repetitive Behavior Scale-Total Score G1: 24.3 ± 24.3 G2: 20.8 ± 16.3 G1 vs G2, p=ns CGI-Severity G1: 3.9 ± 1 G2: 3.6 ± 1 G1 vs G2, p=ns Developmental Behavior Checklist-Total Score G1: 43.9 ± 25.2 G2: 48.2 ± 18 G1 vs G2, p=ns
Nikvarz et al., 2016[96] RCT	Age G1: 6.83 ± 2.98	ABC-Irritability G1: 22.4 ± 11.16	ABC-Irritability G1: 13.5 ± 10.63

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
G1: Memantine (up to 20 mg/day), 16/15 G2: Risperidone (up to 3 mg/day), 18/15 8 weeks/EOT Moderate ROB	G2: 6.56 ± 3.51 IQ NR	G2: 21.26 ± 6.85 ABC-Social Withdrawal/Lethargy G1: 22.13 ± 7.17 G2: 17.53 ± 9.66 ABC-Stereotypic Behavior G1: 5.66 ± 5.7 G2: 5.66 ± 5.97 ABC-Inappropriate Speech G1: 6.27 ± 4.4 G2: 6 ± 2.97 ABC-Hyperactivity G1: 30.4 ± 9.47 G2: 27.53 ± 12.03 CARS-Total Score G1: 42.56 ± 6 G2: 40.16 ± 5.52 CGI-Severity-Mildly Ill G1: 1 (6.7) G2: 0 (0) CGI-Severity-Moderately Ill G1: 1 (6.7) G2: 3 (20) CGI-Severity-Markedly Ill G1: 8 (53.33) G2: 6 (40) CGI-Severity-Severely Ill G1: 5 (33.3) G2: 6 (40)	G2: 9.36 ± 6.29 G1 vs G2, p=ns; ES=0.63 ABC-Social Withdrawal/Lethargy G1: 14.7 ± 8.4 G2: 10.96 ± 6.9 G1 vs G2, p=ns;ES=0.1 ABC-Stereotypic Behavior G1: 4.6 ± 5.06 G2: 3.4 ± 3.86 G1 vs G2, p=ns;ES=0.13 ABC-Inappropriate Speech G1: 4.09 ± 3.44 G2: 3.73 ± 3.07 G1 vs G2, p=ns;ES=0.07 ABC-Hyperactivity G1: 20.3 ± 10.04 G2: 14.53 ± 8.3 G1 vs G2, p=ns;ES=0.37 CARS-Total Score G1: 14.53 ± 8.3 G2: 34.9 ± 5.64 G1 vs G2, p=NS; ES=0.001 CGI-Improvement-Very Much Improved G1: 1 (6.7) G2: 4 (26.7) CGI-Improvement-Much Improved G1: 7 (46.7) G2: 7 (46.7) CGI-Improvement-Minimally Improved G1: 3 (20) G2: 3 (20)

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			CGI-Improvement-No Change G1: 4 (26.7) G2: 1 (6.6) CGI change G1 vs G2, p=ns
Aman et al., 2016[97] RCT G1: Mementine (3-15 mg/day), 60/52 G2: Placebo (ND), 61/50 12 weeks/OLE 42 weeks Low ROB	Age G1: 9 ± 2.2 G2: 8.9 ± 2.2 IQ G1: 77.9 ± 23.1 G2: 75.7 ± 19.4	SRS-Total Raw Score G1: 101.3 ± 25.2 G2: 100.2 ± 21.4	**12 Weeks** SRS-Total Raw Score -7.2 ± 6.6 **42 weeks (OLE)** NR
Arnold et al., 2006[98] RCT G1: Atomoxetine/Placebo (1.4 mg/kg), 16 G2: Placebo/Atomoxetine (1.4 mg/kg), 16 6 weeks/EOT Moderate ROB	Age 9.26 ± 2.93 IQ NR	ABC-Hyperactivity G1: 24.69 ± 13.08 G2: 22.5 ± 12.87 ABC-Irritability G1: 16 ± 9.28 G2: 14.18 ± 9.87 ABC-Social Withdrawal/Lethargy G1: 8.69 ± 9.24 G2: 6.62 ± 8.36 ABC-Stereotypic Behavior G1: 7.37 ± 6.2 G2: 6.19 ± 5.86 ABC-Inappropriate Speech G1: 5.75 ± 3.38 G2: 4.68 ± 2.41 CGI-Severity G1: 4.69 ± 0.6 G2: 4.69 ± 0.6 Repetitive Behavior Scale – Total Score G1: 53.12 ± 22.2 G2: 49.06 ± 21.54	ABC-Hyperactivity G1: 19.31 ± 13.42 G2: 22.37 ± 12.89 G1 vs G2, p=0.04; ES=0.9 ABC-Irritability G1: 13.06 ± 9.28 G2: 14.13 ± 9.89 G1 vs G2, p=ns ABC-Social Withdrawal/Lethargy G1: 6.5 ± 8 G2: 7.43 ± 9.64 G1 vs G2, p=0.01; ES=1.18 ABC-Stereotypic Behavior G1: 4.69 ± 5.84 G2: 6.63 ± 5.8 G1 vs G2, p=ns ABC-Inappropriate Speech G1: 4.87 ± 2.85 G2: 5.43 ± 3.16 G1 vs G2, p=ns Repetitive Behavior Scale – Total Score

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
			G1: 43.5 ± 23.94 G2: 45 ± 5.99 G1 vs G2, p=ns CGI-Improvement G1: 9 (56) G2: 4 (25) G1 vs G2, p=NR
Buspirone			
Chugani et al., 2016[99] RCT G1: Buspirone (2.5 mg), 54/46 G2: Buspirone (5.0 mg), 55/49 G3: Placebo (ND), 57/47 24 weeks/EOT RoB	Age - 2 to < 4 years G1: 25 (46.3) G2: 23 (41.8) G3: 25 (43.9) Age - 4 to < 6 years years G1: 29 (53.7) G2: 32 (58.2) G3: 32 (56.1) IQ NR	ADOS-Composite Total Score G1: 18.3 ± 0.7 G2: 18.4 ± 0.6 G3: 19.6 ± 0.6 ADOS-Social Affect Score G1: 13.9 ± 0.5 G2: 14.2 ± 0.5 G3: 15 ± 0.5 ADOS-Restricted and Repetitive G1: 4.4 ± 0.3 G2: 4.1 ± 0.3 G3: 4.7 ± 0.3 VABS-Social Skills G1: 68.7 ± 1.5 G2: 71 ± 1.5 G3: 70.4 ± 1.5 VABS-Communication G1: 65.5 ± 2.2 G2: 70.6 ± 2.2 G3: 68.5 ± 2.2 ABC-Language Deviance G1: 4.4 ± 0.5 G2: 3.7 ± 0.5 G3: 3.8 ± 0.5 ABC-Anxiety Composite G1: 0.536 ± 0.1 G2: -0.014 ± 0.1 G3: 58.6 ± 3.8 ABC-Social Deviance	ADOS-Composite Total Score G1: 16.2 ± 0.7 G2: 17.9 ± 0.7 G3: 18.6 ± 0.7 ADOS-Social Affect Score G1: 13.3 ± 0.6 G2: 13.4 ± 0.6 G3: 14.1 ± 0.6 ADOS-Restricted and Repetitive G1: 3.5 ± 0.03 G2: 4.6 ± 0.3 G3: 4.4 ± 0.3 VABS-Social Skills G1: 70.4 ± 1.7 G2: 72.3 ± 1.7 G3: 72.4 ± 1.7 VABS-Communication G1: 68.2 ± 2.3 G2: 72.7 ± 2.2 G3: 69.7 ± 2.2 ABC-Language Deviance G1: 4.4 ± 0.5 G2: 3.7 ± 0.5 G3: 3.8 ± 0.5 ABC-Anxiety Composite G1: 0.118 ± 0.1 G2: -0.12 ± 0.1 G3: -0.242 ± 0.1 ABC-Social Deviance

Author, Year Study Design Groups (dose), N enrollment / N final Treatment duration/Follow-up timepoint post-treatment Risk of Bias	Mean age, years ± SD Mean IQ ±SD	Outcome measure/Baseline scores, mean ±SD	Outcome measure/Post-treatment scores, mean ± SD
		G1: 15.3 ± 1.2 G2: 11.8 ± 1.2 G3: 14.2 ± 1.2 Repetitive Behavior Scale-Total Score G1: 46.9 ± 3.5 G2: 31.5 ± 3.5 G3: 36.7 ± 3.5 CYBOCS-Total Score G1: 12.1 ± 0.6 G2: 11.5 ± 0.6 G3: 11.9 ± 0.6 Sensory Processing Measure-Total Score G1: 58.6 ± 3.8 G2: 67.2 ± 3.7 G3: 65.4 ± 3.7	G1: 12.1 ± 1.1 G2: 10.6 ± 1.1 G3: 11 ± 1.1 Repetitive Behavior Scale-Total Score G1: 38 ± 3.3 G2: 29.9 ± 3.3 G3: 34.2 ± 3.2 CYBOCS-Total Score G1: 11.1 ± 0.6 G2: 10.7 ± 0.6 G3: 11.2 ± 0.6 Sensory Processing Measure-Total Score G1: 59.6 ± 3.6 G2: 68.1 ± 3.5 G3: 66.7 ± 3.6

ABC-Aberrant Behavior Checklist; CGI-Clinical Global Impression; VABS-Vineland Adaptive Behavior Scale; CYBOCS-Children's Yale-Brown Obsessive Compulsive Scale; EOT-End of Treatment; SRS-Social Responsiveness Scale ; SDB-sleep-disordered breathing ; PLS-Preschool Language Scale ; EOWPVT-Expressive One Word Vocabulary Test ; CSHQ- ; DS-duration of sleep ; TST-Total Sleep Time ; CARS-Childhood Autism Rating Scale ; ADOS-Autism Diagnostic Observation Schedule ; ATEC-Autism Treatment Evaluation Checklist ; CGIS-Clinical Global Impression-Severity ; SOD-sleep onset delay; CGAS- Children's Global Assessment Scale; SOL-sleep onset latency ; WASO-wake after sleep onset ; SE-sleep efficiency; DBC-Developmental Behavior Checklist ; GHQ-General Health Questionnaire ; OSU- ; OACIS- ; OARS- ; RBS- ; EVT- ; EEG-electroencephalogram ; FMAER- frequency modulated auditory evoked response