

Table S1. Change in number of miRNAs significantly differentially expressed after sensitivity analyses.

		ANT				N-back	Conner's			CBCL	New significant miRNAs
		HRT-SE	Zeros	Omissions	Conflict	3 numbers	ADHD Index	Inattention	Hyperactivity	ADHD	
Sex	Each separately:										
	Female							0	0		
	Male							1D, 1UP	4D		
SES	(as covariate)							1D, 2UP	26D		
Cohort	One removed:										
	BIB							0	15D		Hyper.: miR-378a-3p
	EDEN							1D	28D		Hyper.: miR-126-3p, 425-5p, 15a-5p, 199a-3p
	INMA				1D			0	0		Conflict: miR-6812-5p
	KANC							1D, 5UP	16D	3UP	Inatt.: miR-4687-3p, 4788, 7152-3p CBCL: miR-1268b, 4763-3p, 1268a
	MOBA							0	25D		
	RHEA							1D, 2UP	0		
Cohort	Each separately:										
	BIB							0	0		
	EDEN							0	0		
	INMA							0	7D		Hyper.: miR-378a-3p
	KANC						2UP	0	0		ADHD I.: miR-4749-3p, 6875-5p
	MOBA							0	0		
	RHEA							0	0		
Round	(as covariate)							1D, 2UP	28D		
Round	Each separately:										
	Round 1						1UP	1UP	0		ADHD I.: miR-4443
	Round 2							0	0		

D, downregulated; UP, upregulated.

Table S2. miRNAs linked to ADHD in previous literature.

miRNA	Status in ADHD	Sample type	References
hsa-let-7d	Upregulated (two studies)	Serum	(1, 2)
hsa-let-7d	Downregulated	WB	(3)
hsa-let-7g-5p	ADHD-prediction model	WBCs	(4)
hsa-let-7g-5p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-101-3p	ADHD-prediction model	WBCs	(4)
hsa-miR-101-3p	Upregulated	Serum	(6)
hsa-miR-101-3p	Decreased in both responder and non-responder patient group after MPH treatment	WBCs	(5)
hsa-miR-106b-5p	Downregulated	Serum	(6)
hsa-miR-106b-5p	Downregulated	WB	(7)
hsa-miR-107	Downregulated	WB	(7)
hsa-miR-124-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-125a-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-126-5p	ADHD-prediction model	WBCs	(4)
hsa-miR-126-5p	Upregulated	WBCs	(9)
hsa-miR-126-5p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-129-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-130a-3p	Upregulated	Serum	(6)
hsa-miR-132-3p	Upregulated	Plasma	(10)
hsa-miR-138-5p	Upregulated	Serum	(6)
hsa-miR-1-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-140-3p	ADHD-prediction model	WBCs	(4)
hsa-miR-140-3p	Upregulated	WBCs	(9)
hsa-miR-140-3p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-142-3p	Downregulated in ADHD group when presence of psychiatric disease in their families.	Plasma	(11)
hsa-miR-142-5p	ADHD-prediction model	WBCs	(4)
hsa-miR-148b-3p	Downregulated	WB	(12)
hsa-miR-150-5p	ADHD-prediction model	WBCs	(4)
hsa-miR-150-5p	Increased in patient group not responding to MPH treatment	WBCs	(5)
hsa-miR-151a-3p	ADHD-prediction model	WBCs	(4)
hsa-miR-151a-3p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-151a-5p	ADHD-prediction model	WBCs	(4)

hsa-miR-151a-5p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-155-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-155-5p	Upregulated	WB	(7)
hsa-miR-15a-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-16-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-17-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-185-5p	Downregulated	PBMCs	(13)
hsa-miR-18a-5p	Downregulated	WB	(7)
hsa-miR-191-5p	Upregulated	PBMCs	(13)
hsa-miR-195-5p	Upregulated	Serum	(6)
hsa-miR-19a-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-19b-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-204-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-21-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-223-3p	ADHD-prediction model	WBCs	(4)
hsa-miR-22-3p	Downregulated	WB	(7)
hsa-miR-22-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-24-3p	Downregulated	WB	(7)
hsa-miR-24-3p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-26b-5p	Downregulated	PBMCs	(13)
hsa-miR-27a-3p	ADHD-prediction model	WBCs	(4)
hsa-miR-27a-3p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-30a-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-30e-5p	ADHD-prediction model	WBCs	(4)
hsa-miR-30e-5p	Upregulated	WBCs	(9)
hsa-miR-30e-5p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-335-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-34a-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-34c-3p	Upregulated	PBMCs	(14)
hsa-miR-378a-5p	Downregulated in ADHD group when presence of psychiatric disease in their families.	Plasma	(11)
hsa-miR-4281	ADHD-prediction model + downregulated. Increased after 12-week MPH treatment.	Serum	(15)
hsa-miR-4466	ADHD-prediction model + upregulated. Decreased after 12-week MPH treatment.	Serum	(15)
hsa-miR-4516	ADHD-prediction model + downregulated. Increased after 12-week MPH treatment.	Serum	(15)

hsa-miR-4763-3p	ADHD-prediction model + downregulated. Increased after 12-week MPH treatment.	Serum	(15)
hsa-miR-486-5p	ADHD-prediction model	WBCs	(4)
hsa-miR-486-5p	Decreased in patient group responding to MPH treatment	WBCs	(5)
hsa-miR-5692b	Upregulated	WB	(3)
hsa-miR-6090	ADHD-prediction model + downregulated. Increased after 12-week MPH treatment.	Serum	(15)
hsa-miR-616-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-652-3p	Upregulated	WB	(12)
hsa-miR-92a-3p	ADHD-prediction model	WBCs	(4)
hsa-miR-942-5p	Upregulated	WB	(12)
hsa-miR-9-5p	Targeting ADHD gene set	Predicted	(8)
hsa-miR-96-5p	Targeting ADHD gene set	Predicted	(8)

WB, whole blood; WBCs, white blood cells; PBMCs, peripheral blood mononuclear cells; MPH, methylphenidate.

Table S3. Functional enrichment analysis of 29 miRNAs significantly associated with hyperactivity.

KEGG pathway	#miRNAs	#genes	p value
Proteoglycans in cancer	27	159	5.36e-22
Viral carcinogenesis	27	157	6.46e-15
Renal cell carcinoma	27	60	2.71e-11
Hippo signaling pathway	27	114	4.86e-11
Protein processing in endoplasmic reticulum	27	128	7.47e-09
ECM-receptor interaction	25	51	1.11e-07
Cell cycle	27	97	1.11e-07
Ubiquitin mediated proteolysis	27	109	2.55e-07
Endocytosis	27	152	2.92e-07
TGF-beta signaling pathway	27	61	3.32e-07
Adherens junction	27	61	4.08e-07
Estrogen signaling pathway	27	74	5.94e-07
Hepatitis B	27	104	6.86e-07
Glioma	26	51	7.97e-07
Prostate cancer	27	72	1.35e-06
Chronic myeloid leukemia	26	60	2.07e-06
Fatty acid metabolism	22	33	2.99e-06
Thyroid hormone signaling pathway	27	88	2.99e-06
Signaling pathways regulating pluripotency of stem cells	27	103	3.01e-06
Pathways in cancer	27	268	3.58e-06
Oocyte meiosis	27	82	8.49e-06
Colorectal cancer	27	51	1.06e-05
Glycosaminoglycan biosynthesis - keratan sulfate	19	12	1.26e-05
p53 signaling pathway	27	54	2.38e-05
Pancreatic cancer	26	52	2.69e-05
Bacterial invasion of epithelial cells	26	59	2.82e-05
N-Glycan biosynthesis	25	37	3.60e-05

FoxO signaling pathway	27	98	3.73e-05
AMPK signaling pathway	27	93	5.67e-05
Prion diseases	25	21	9.46e-05
Bladder cancer	26	33	9.60e-05
Focal adhesion	27	144	1.23e-04
Sphingolipid signaling pathway	26	84	1.24e-04
Small cell lung cancer	27	66	1.26e-04
Endometrial cancer	26	42	1.31e-04
Thyroid cancer	25	24	1.33e-04
Non-small cell lung cancer	25	43	2.35e-04
Epstein-Barr virus infection	27	140	2.94e-04
Lysine degradation	26	34	3.04e-04
ErbB signaling pathway	27	64	3.28e-04
mTOR signaling pathway	27	48	4.31e-04
HIF-1 signaling pathway	27	79	4.58e-04
Other types of O-glycan biosynthesis	24	20	6.03e-04
Transcriptional misregulation in cancer	27	116	8.72e-04
Progesterone-mediated oocyte maturation	25	65	1.50e-03
Toxoplasmosis	27	84	1.60e-03
HTLV-I infection	27	172	1.60e-03
Central carbon metabolism in cancer	27	51	1.67e-03
Regulation of actin cytoskeleton	27	139	1.70e-03
TNF signaling pathway	26	79	1.76e-03
Spliceosome	27	92	1.97e-03
Neurotrophin signaling pathway	27	84	2.80e-03
Chagas disease (American trypanosomiasis)	27	70	3.84e-03
RNA transport	27	112	4.49e-03
Axon guidance	27	85	4.49e-03
Acute myeloid leukemia	26	43	4.87e-03
Insulin signaling pathway	27	96	4.95e-03

Fatty acid degradation	21	25	5.18e-03
Prolactin signaling pathway	26	51	5.24e-03
Wnt signaling pathway	26	91	5.25e-03
Fatty acid elongation	17	13	5.80e-03
Shigellosis	25	46	6.33e-03
Gap junction	26	58	7.53e-03
Steroid biosynthesis	19	14	7.74e-03
Pathogenic Escherichia coli infection	26	41	8.92e-03
Inositol phosphate metabolism	27	42	8.93e-03
Melanoma	27	49	8.93e-03
RNA degradation	26	54	9.03e-03
Glycosaminoglycan biosynthesis - heparan sulfate / heparin	22	17	1.16e-02
mRNA surveillance pathway	27	65	2.97e-02
Platelet activation	26	82	3.03e-02
Terpenoid backbone biosynthesis	21	16	3.19e-02
Fatty acid biosynthesis	22	7	3.44e-02
Apoptosis	27	59	4.02e-02
Lysosome	25	78	4.53e-02
Adrenergic signaling in cardiomyocytes	27	85	4.92e-02

Table S4. Functional enrichment analysis of 15 miRNAs associated with hyperactivity/ADHD in this and previous studies.

KEGG pathway	#miRNAs	#genes	p value
Proteoglycans in cancer	14	149	1.08e-26
Viral carcinogenesis	14	140	1.08e-12
Hippo signaling pathway	14	106	2.08e-12
Protein processing in endoplasmic reticulum	14	118	3.76e-09
Endocytosis	14	141	7.57e-08
Signaling pathways regulating pluripotency of stem cells	14	98	1.47e-07
Glioma	13	48	2.53e-07
Adherens junction	14	55	2.53e-07
Renal cell carcinoma	14	53	3.52e-07
TGF-beta signaling pathway	14	56	3.66e-07
Cell cycle	14	89	4.72e-07
Ubiquitin mediated proteolysis	14	99	6.56e-07
Thyroid hormone signaling pathway	14	82	1.04e-06
AMPK signaling pathway	14	89	2.16e-06
Bacterial invasion of epithelial cells	14	57	2.68e-06
Chronic myeloid leukemia	14	55	3.45e-06
Pancreatic cancer	14	49	4.45e-06
Non-small cell lung cancer	13	42	1.19e-05
Pathways in cancer	14	240	1.60e-05
Sphingolipid signaling pathway	14	79	1.72e-05
Hepatitis B	14	91	1.96e-05
Bladder cancer	14	32	1.96e-05
Oocyte meiosis	14	77	2.23e-05
Prion diseases	13	18	2.66e-05
mTOR signaling pathway	14	47	2.91e-05
FoxO signaling pathway	14	90	3.41e-05
N-Glycan biosynthesis	14	34	4.26e-05

Estrogen signaling pathway	14	67	4.26e-05
Prostate cancer	14	63	4.33e-05
Glycosaminoglycan biosynthesis - keratan sulfate	12	10	4.36e-05
p53 signaling pathway	14	50	4.36e-05
Endometrial cancer	13	39	1.10e-04
Central carbon metabolism in cancer	14	48	1.33e-04
Insulin signaling pathway	14	93	1.64e-04
Colorectal cancer	14	44	1.74e-04
Lysine degradation	14	32	2.03e-04
RNA transport	14	106	2.96e-04
Focal adhesion	14	129	3.27e-04
Thyroid cancer	13	22	4.61e-04
Small cell lung cancer	14	59	5.61e-04
Steroid biosynthesis	11	14	7.23e-04
ECM-receptor interaction	14	45	7.23e-04
Other types of O-glycan biosynthesis	12	19	7.29e-04
Progesterone-mediated oocyte maturation	13	60	9.75e-04
Shigellosis	13	44	9.93e-04
HIF-1 signaling pathway	14	71	1.00e-03
Fatty acid elongation	10	11	1.19e-03
Prolactin signaling pathway	13	47	1.19e-03
Fatty acid metabolism	13	29	1.54e-03
TNF signaling pathway	13	72	1.54e-03
Gap junction	14	54	1.72e-03
Spliceosome	14	82	2.06e-03
Fatty acid biosynthesis	13	7	2.49e-03
Pathogenic Escherichia coli infection	14	39	2.97e-03
RNA degradation	14	51	4.24e-03
ErbB signaling pathway	14	56	4.37e-03
Neurotrophin signaling pathway	14	76	4.54e-03

Regulation of actin cytoskeleton	14	123	4.66e-03
Axon guidance	14	78	5.30e-03
Chagas disease (American trypanosomiasis)	14	63	5.30e-03
Melanoma	14	45	5.33e-03
Terpenoid backbone biosynthesis	12	16	5.35e-03
Wnt signaling pathway	14	81	5.53e-03
Transcriptional misregulation in cancer	14	100	6.98e-03
mRNA surveillance pathway	14	61	7.36e-03
Glycosaminoglycan biosynthesis - heparan sulfate / heparin	14	15	9.11e-03
HTLV-I infection	14	150	1.27e-02
Lysosome	14	73	1.49e-02
Adrenergic signaling in cardiomyocytes	14	76	1.49e-02
Platelet activation	13	75	1.69e-02
VEGF signaling pathway	13	40	1.92e-02
Inositol phosphate metabolism	14	38	1.92e-02
Acute myeloid leukemia	13	37	2.09e-02
Circadian rhythm	13	22	2.54e-02
Epstein-Barr virus infection	14	117	2.84e-02
Toxoplasmosis	14	70	3.50e-02
Non-alcoholic fatty liver disease (NAFLD)	14	85	4.23e-02
Vitamin B6 metabolism	3	5	4.57e-02
Vasopressin-regulated water reabsorption	14	32	4.82e-02

Table S5. MiRNAs statistically significant for Conner’s hyperactivity or inattention score, and their previous associations with neurodevelopmental or psychiatric phenotypes.

ADHD-trait	miRNA	ADHD	ASD	SZ	MDD	BD	References
Hyperactivity							
	hsa-let-7c-5p				✓		MDD (16)
	hsa-let-7i-5p						
	hsa-miR-101-3p	✓	✓		✓		ADHD (4, 6), ASD (17), MDD (18, 19)
	hsa-miR-103a-3p		✓				ASD (20)
	hsa-miR-106b-5p	✓	✓	✓		✓	ADHD (6, 7), ASD (21), SZ (22, 23), BD (24, 25)
	hsa-miR-107	✓	✓	✓	✓	✓	ADHD (7), ASD (26), SZ (24), MDD (24), BD (25)
	hsa-miR-130a-3p	✓	✓	✓			ADHD (6), ASD (17), SZ (22)
	hsa-miR-140-3p	✓	✓			✓	ADHD (4, 9), ASD (27), BD (19)
	hsa-miR-142-3p	✓	✓		✓	✓	ADHD (11), ASD (26), MDD (24), BD (28)
	hsa-miR-144-3p		✓				ASD (29)
	hsa-miR-146b-5p		✓	✓			ASD (26, 30), SZ (31)
	hsa-miR-148b-3p	✓	✓	✓			ADHD (12), ASD (26), SZ (22)
	hsa-miR-150-5p	✓	✓	✓			ADHD (4), ASD (32), SZ (24)
	hsa-miR-181a-5p		✓	✓			ASD (26), SZ (22)
	hsa-miR-181b-5p		✓	✓			ASD (26), SZ (19, 33, 34)
	hsa-miR-186-5p		✓	✓		✓	ASD (26), SZ (35), BD (35)
	hsa-miR-19a-3p	✓	✓		✓		ADHD (8), ASD (26, 32), MDD (36)
	hsa-miR-19b-3p	✓	✓	✓	✓	✓	ADHD (8), ASD (26), SZ (37), MDD (38), BD (39)
	hsa-miR-24-3p	✓		✓	✓		ADHD (7, 8), SZ (22), MDD (19)
	hsa-miR-27a-3p	✓	✓	✓			ADHD (4), ASD (26), SZ (22)
	hsa-miR-29a-3p		✓	✓		✓	ASD (40), SZ (41), BD (24, 25)
	hsa-miR-29b-3p		✓	✓			ASD (26), SZ (22)
	hsa-miR-29c-3p			✓		✓	SZ (24), BD (24)
	hsa-miR-30e-5p	✓	✓	✓			ADHD (4, 9), ASD (21), SZ (19)
	hsa-miR-324-5p						

	hsa-miR-342-5p				✓	MDD (19)
	hsa-miR-378i					
	hsa-miR-92a-3p	✓	✓	✓	✓	ADHD (4), ASD (26), SZ (42, 43), MDD (19)
	hsa-miR-942-5p	✓				ADHD (12)
Inattention						
	hsa-miR-3180-3p					
	hsa-miR-4257					
	hsa-miR-4443				✓	ASD (26)

Not an exhaustive list. ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; SZ, schizophrenia; MDD, major depression disorder; BD: bipolar disorder.

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