## **Supplement to:**

Enhanced nitric oxide (NO) and decreased ADMA synthesis in pediatric ADHD and selective potentiation of NO synthesis by methylphenidate

Kathrin Jansen<sup>1\*</sup>, Beatrice Hanusch<sup>1\*</sup>, Saskia Pross<sup>1,2</sup>, Erik Hanff<sup>3</sup>, Kathrin Drabert<sup>3</sup>, Alexander Bollenbach<sup>3</sup>, Irina Dugave<sup>1,4</sup>, Christina Carmann<sup>1</sup>, Rainer Georg Siefen<sup>1</sup>, Barbara Emons<sup>5,6</sup>, Georg Juckel<sup>5,6</sup>, Tanja Legenbauer<sup>7</sup>, Dimitrios Tsikas<sup>3‡</sup>, Thomas Lücke<sup>1‡</sup>

**Table S1** Plasma concentrations (median [25<sup>th</sup> – 75<sup>th</sup> interquartile range]) of ADMA, arginine (Arg), nitrate, and nitrite of controls (Co) and ADHD children without (-MPH) and with (+MPH) methylphenidate (MPH) medication

	Control	-MPH	+MPH	Statistics	P
ADMA (μM)	0.57 [0.51-0.66]	0.50 [0.46-0.54]	0.49 [0.46-0.54]	Co/-MPH: z = -18.9 Co/+MPH: z = -19.4 -MPH/+MPH: z = 0.60	.008 .01 .99
Arg (μM)	73.8 ± 17.3	68.1 ± 14.3	65.2 ± 14.1	F(2,78) = 2.16	.12
Nitrate (µM)	30.8 [27.0-37.6]	49.9 [44.8-53.5]	53.0 [44.1-55.4]	Co/-MPH: <i>z</i> = 23.1 Co/+MPH: <i>z</i> = 25.2 -MPH/+MPH: <i>z</i> = -2.17	<.001 <.001 .99
Nitrite (µM)	2.12 [0.83-2.32]	2.44 [2.13-2.8]	3.1 [2.78-3.5]	Co/-MPH: <i>z</i> = 16.7 Co/+MPH: <i>z</i> = 35.8 -MPH/+MPH: <i>z</i> = -19.1	.01 <.001 <.001

Normally distributed data (mean ± SDstandard deviation) were calculated with one-way ANOVA; non-normally distributed data (median [25<sup>th</sup> – 75<sup>th</sup> interquartile range]) with Kruskal-Wallis test; corresponding test statistics: *F*-value (between group df, within-group df), *z*-score. Arg, Arginine; ADMA, Asymmetric dimethylarginine.

**Table S2** Age-corrected ADMA and nitrite plasma concentrations in ADHD children without (-MPH) and with (+MPH) methylphenidate (MPH) medication

	-MPH		+MPH			
	Meanadj ± SEM	95% CI	Mean <sub>adj</sub> ± SEM	95% CI	Statistics	P
ADMA (μM)	$0.50 \pm 0.01$	[0.48; 0.53]	0.51 ± 0.01	[0.48; 0.54]	F(1,37) = 0.82	.77
Nitrite (µM)	2.67 ± 0.15	[2.38; 2.97]	$3.16 \pm 0.16$	[2.84; 3.48]	F(1,39) = 5.15	.03

One-way ANCOVA adjusted for age. <u>ADMA, Asymmetric dimethylarginine;</u> Mean<sub>adj</sub>, adjusted mean; SEM, standard error of the mean; *F*-value (between group df, within-group df).

**Table S3** Age-corrected ADMA and nitrite plasma concentration (mean $_{\rm adj}$  (SEM) in ADHD children without (-MPH) and with (+MPH) methylphenidate (MPH) medication according to the IQ range of 50 – 100 and above 100 (>100)

	-MPH		+MPH			
IQ	50-100 (n = 3)	>100 (n = 8)	50-100 (n = 9)	>100 (n = 5)	Statistics	P
ADMA (μM)	0.46 (0.02)	0.51 (0.01)	0.53 (0.01)	0.46 (0.02)	MPH: F(1,20) = 0.41 IQ: F(1,20) = 0.17 MPH×IQ: F(1,20) = 12.4	.53 .68 .002
Nitrite (µM)	2.45 (0.40)	3.01 (0.24)	3.10 (0.22)	3.22 (0.27)	MPH: F(1,21) = 2.14 IQ: F(1,21) = 1.12 MPH×IQ: F(1,21) =	.16 .30 .47

mean; SEM, standard error of the mean; *F*-value (between group df, within-group df).