Attention-Deficit/Hyperactivity Disorder Remission Is Linked to Better Neurophysiological Error Detection and Attention-Vigilance Processes

Supplement 1

Further Details on the Task

The version of Eriksen flanker task used in this study consisted of 10 blocks of 40 trials where congruent versus incongruent conditions and the direction of responses (left versus right) were counter-balanced and randomized. Participants were seated on an adjustable chair in an acoustically shielded, video-monitored room. Two practice blocks were administered before the task blocks and task comprehension was ascertained prior to task performance. On congruent trials, flanker and target arrowheads pointed in the same direction; on incongruent trials, they pointed in opposite directions. Flankers were presented every 1650 ms (inter-trial interval (ITI), therefore an inter-block interval (IBI) was 1400 ms). ITI and IBI were fixed. After each block, feedback was presented on screen to emphasize both speed and accuracy, in order to encourage participants to make enough errors to enable analysis of ERN/Pe components, and enough correct responses for analysis of the N2. Where participants made > 10% errors on congruent or > 40% errors on incongruent trials, they were instructed to slow down. Where participants made < 10% errors on congruent or < 40% errors on incongruent trials, they were instructed to perform faster. If neither rule applied, feedback informed participants to continue the same way. The task was run during a 1.5-hour recording session between two other tasks not reported here: preceded by the Continuous Performance Test-OX and followed by the Fast Task (see (1) for details). Breaks of at least 5 minutes were given in between tasks. Where necessary, participants were told to minimize movement or blinking.

Comparison Between Peak-to-Peak and Peak-to-Baseline ERN

In the present study the ERN was measured with reference to the previous preceding positive peak (the PNe, occurring between -100 and 50ms), consistently with several previous studies in the Michelini et al.

Supplement

literature (2-8). In these studies, this measurement of the ERN has proven useful to account for individual variability in amplitude range and to reduce latent low-frequency noise. The peak-to-peak ERN measure is also a robust index of early error processing, which has been shown to delineate ADHD from controls in independent samples using this version of the Eriksen flanker task (9-11). Since some previous studies on ADHD samples have instead measured the ERN as a peak-to-baseline measure (12-14), we also investigated the differences between ADHD remitters, persisters and controls on this peak-to-baseline measure and on the PNe directly, for completeness and to allow comparison with previous results.

For the peak-to-baseline ERN we found significant overall group differences (p=.05) and ADHD persisters vs. controls difference (p<.01), but ADHD remitters did not significantly differ from either persisters (p=.47) or controls (p=.34). We did not find any group differences on the PNe (overall group effect: p=.18; ADHD remitters vs. persisters: p=.27; ADHD remitters vs. controls: p=.69; ADHD persisters vs. controls: p=.14).

Considering these results, the peak-to-baseline ERN may be less sensitive to ADHD remission/persistence compared to the peak-to-peak ERN. Of note, the analysis of PNe alone showed no group differences on this measure, thus the inclusion of this earlier peak in the peak-to-peak measure of the ERN did not explain the group differences on the peak-to-peak ERN, which reflect the voltage change from the PNe to the negative ERN.

		Pearson <i>r</i> with age	
-	Controls	ADHD-R	ADHD-P
Congruent errors	0.01	-0.19	-0.23*
Incongruent errors	-0.14†	-0.27	-0.29*
Congruent MRT (ms)	0.13	0.02	0.17
Incongruent MRT (ms)	-0.15†	-0.02	-0.20†
Congruent RTV (ms)	0.18*	0.07	0.23*
Incongruent RTV (ms)	0.25**	0.05	0.18
N2 at Fz (µV)	-0.42**	-0.41†	-0.39*
N2 at FCz (µV)	-0.28**	-0.03	-0.15
ERN (peak) at FCz (µV)	-0.25**	0.19	-0.09
ERN (peak-to-peak) at FCz (µV)	-0.12	0.10	0.07
Pe at CPz (μV)	-0.36**	-0.46*	-0.25*

Table S1. Pearson correlations between cognitive and ERP measures and age, divided by group

ADHD-R = ADHD remitters; ADHD-P = ADHD persisters; Congruent = congruent condition; Incongruent = incongruent condition; MRT = reaction time of correct response to targets; RTV = reaction time variability to targets (SD of reaction time).

***p*≤.01; **p*≤.05; †*p*<.09.

	Group	Group effect		Congruency effect		ongruency	Site	effect	Group*Site		
	Z	р	Z	р	Z	р	Z	р	Z	р	
Errors	7.95	<.01**	43.39	<.01**	-5.22	<.01**	-	-	-	-	
MRT	0.16	.87	582.71	<.01**	2.91	<.01**	-	-	-	-	
RTV	-10.24	<.01**	-90.07	<.01**	6.95	<.01**	-	-	-	-	
N2	2.64	<0.01**	9.65	<.01**	33	.74	83.22	<0.01**	-3.36	<0.01**	

Table S2. Full results of mixed model analyses showing main effects of group, condition (congruency), site (for the N2 only), and interaction effects on cognitive-performance and ERP measures

MRT = reaction time of correct response to targets; RTV = reaction time variability to targets (SD of reaction time).

Data on performance measures were available for the full sample (87 ADHD-P, 23 ADHD-R and 169 controls); data on the N2 were available for 84 ADHD-P, 23 ADHD-R and 169 controls. Age was also included as a covariate and its effects not presented here for simplicity, but available on request. Only group effects were tested on the ERN and Pe, thus regression models (rather than mixed models) were used and the full results are presented in Table 2 of the main test.

**p≤.01; *p≤.05; †p<.09.

Table S3. Descriptive statistics and group comparison on cognitive-performance and ERP measures performed only on ma
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	ADHD-P	ADHD-R mean (SD)	Ctrl mean (SD)	Group Comparison							
	mean (SD)			р	ADHD-P vs Ctrl		ADHD-P vs ADHD-R		ADHD-R vs Ctrl		
					d	р	d	р	d	р	
Performance											
Congruent errors	9.59	4.00	4.01	<.01**	.73	<.01**	.68	.01**	.00	.97	
	(13.570	(3.85)	(7.10)								
Incongruent errors	57.96	56.22	50.66	<.01**	.46	<.01**	.09	.81	.35	.13	
	(18.59)	(20.75)	(18.69)								
Congruent MRT (ms)	352.47	339.58	332.45	<.01**	.42	<.01**	.19	.43	.23	.32	
	(62.91) (38.99)	(38.99)	(33.08)								
Incongruent MRT (ms)	448.12	441.94	428.37	<.01**	.41	<.01**	.02	.95	.42	.02*	
	(59.19)	(33.44)	(41.89)								
Congruent RTV (ms)	113.94	83.19	74.40	<.01**	.99	<.01**	.53	.01**	.43	.05*	
	(70.72) (28.22)	(28.22)	(19.75)								
Incongruent RTV (ms)	121.34	88.18	75.51	<.01**	.97	<.01**	.45	.05*	.53	.02*	
	(86.84)	(32.91)	(22.99)								
ERPs											
N2 at Fz (µV)	-7.33	-6.91	-6.50	.02*	.34	.10	.05	.64	.29	.05*	
	(3.74)	(3.61)	(3.30)								
N2 at FCz (µV)	-5.91	-6.26	-7.04	.09†	.26	.11	.14	.30	.12	.85	
	(3.89)	(3.57)	(3.92)								

	ADHD-P mean (SD)	ADHD-R mean (SD)	Ctrl mean (SD)	Group Comparison						
				р	ADHD-P vs Ctrl		ADHD-P vs ADHD-R		ADHD-R vs Ctrl	
					d	р	d	р	d	р
ERN at FCz (peak-to-	-7.97	-9.64	-9.99	<.01**	.52	<.01**	.47	.09†	.06	.78
peak, µV)	(3.38)	(4.11)	(4.12)							
Pe at CPz (µV)	9.67	10.96	11,50	.02*	.41	.02*	.38	.11	.04	.91
	(4.14)	(4.06)	(4.45)							

ADHD-P = ADHD persisters, ADHD-R = ADHD remitters, Ctrl = Control group, SD = standard deviation, p = regression model significant testing, d = Cohen's d effect size (0.2 small, 0.5 medium and 0.8 large), Congruent = congruent condition, Incongruent = incongruent condition, MRT = reaction time of correct response to targets, RTV = reaction time variability to targets (i.e. SD of reaction time).

Data on performance measures and N2 were available for 72 ADHD-P, 23 ADHD-R and 128 controls; data on the ERN and Pe were available for 69 ADHD-P, 19 ADHD-R and 111 controls.

Age was included as a covariate in all analyses and its effects are not presented here for simplicity, but available on requests.

Bold denotes a large effect size, italics denotes a medium effect size.

**p≤.01; *p≤.05; †p≤.09.



Figure S1. Difference wave (in blue) showing the difference between ADHD persisters (ADHD-P, in red) and control participants (Controls, in black) in grand average stimulus-locked ERPs of the N2 at Fz and FCz electrodes between 250-450 ms after incongruent stimuli where a correct response was made, with t-map. Topographical differences between ADHD persisters and controls can be observed here, which likely led to an enhanced N2 in persisters at Fz but with a trend for reduction at FCz. This is indicated in the grand average ERP showing the difference wave (in blue, ADHD persisters minus controls), which appears in the positive region of the graph at Fz (corresponding to the positive frontal difference in yellow-red in the t-map) and in the negative region of the graph at FCz (corresponding to the negative central difference in blue in the t-map).

Supplemental References

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