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RESEARCH

Altered Error Monitoring and Decreased Flanker Task Accuracy in Pediatric Obsessive–Compulsive Disorder

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Abstract

The error-related negativity (ERN) and error positivity (Pe) are components of the event-related potential following an error that are potential mechanistic biomarkers of obsessive–compulsive disorder (OCD). The study examined the ERN, Pe, flanker task accuracy, and clinical measures in 105 OCD cases and 105 matched healthy controls (HC) ages 8–18 years. Higher flanker task accuracy in all participants was associated with an increased ERN amplitude and increased difference between Pe and correct positivity amplitudes (ΔPe). Compared to HC, OCD cases had an increased ERN but *decreased* ΔPe and flanker task accuracy. Those differences were also significant in tic-related and non-tic-related OCD cases compared to HC. A lower ΔPe was associated in cases with an earlier age at OCD symptom onset. The results support the hypothesis that OCD involves defects in an error monitoring system and suggest a reduced ΔPe may compromise error signaling and cause uncertainty about the correctness of a response.

Keywords Error positivity · Error-related negativity · Flanker task · Obsessive–compulsive disorder · Tic disorder · Youth

Introduction

Obsessive–compulsive disorder (OCD) is a heterogeneous and often chronic psychiatric disorder, with lifetime prevalence rates ranging from 1 to 3% [1]. OCD has a median age at onset of about 19 years, with about 25% of cases starting by 14 years [2]. OCD involves recurrent intrusive thoughts and repetitive behaviors or mental acts that vary in their content and are often associated with other psychiatric disorders [1]. About 22% of pediatric OCD cases have a comorbid tic disorder [3], with tic-related OCD (TR OCD) having an earlier age at onset than non-tic-related OCD (NTR OCD) [4].

Research on mechanistic biomarkers that precede or develop concurrently with onset of pediatric OCD may clarify its pathogenesis, improve diagnostic and preventive strategies, and provide treatment targets [5]. OCD has been hypothesized to involve persistent errors signals that cannot be eliminated by behavioral output [6]. Performance monitoring in the context of cognitive control refers to neural processes that support the continuous monitoring of thoughts and actions [7, 8]. Two components of the event-related potential (ERP) involved in performance monitoring are the error-related negativity (ERN or Ne), a negative deflection in the response-locked ERP waveform that peaks within 100 ms after error commission and is maximal at frontocentral electrodes, and the error positivity (Pe), a positive deflection in the response-locked ERP waveform that peaks between 200 and 500 ms after an erroneous response and is maximal at centroparietal electrodes [7–11]. The correct response negativity (CRN) and correct positivity (Pc) that occur after a correct response in the same time windows as the ERN and Pe, respectively, are distinguished from their counterparts by having lower amplitudes [7–11].

The ERN has been described as a neural marker of error monitoring processes [7–10], reinforcement learning [12], error-related distress [13], and the motivational significance of errors [14]. Thus, it is a unit of analysis in three domains of the Research Domain Criteria project: cognitive systems (cognitive control: performance monitoring), negative valence systems (sustained threat), and positive valence systems (reward learning) [15]. The ERN increases

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in magnitude throughout childhood and adolescence, indicating a prolonged maturation of the system underlying performance monitoring that may allow the ERN to adjust to defects in that system over time [6, 16].

An increased ERN amplitude has been found in studies of adults and children with OCD using choice reaction time tasks eliciting response conflict, including a meta-analysis with 39 studies, indicating the ERN may serve as a biomarker for OCD [7, 8, 15, 17–19]. Studies with an enlarged ERN in adults with OCD have noted either normal or increased accuracy on response conflict tasks relative to healthy controls (HC) [7, 8, 15, 17–19]. However, our studies of older children and adolescents have shown increased ERN amplitudes but *decreased* flanker task accuracy in youth with OCD compared to HC [20, 21]. In contrast, we found an augmented ERN amplitude but normal flanker task accuracy in youth with anxiety disorders compared to HC [22] and no differences between youth with major depressive disorder and HC in either ERN amplitude or flanker task accuracy [21].

The inconsistency between an enlarged ERN and decreased task accuracy suggests an altered Pe may compromise performance monitoring in pediatric OCD [11]. The Pe has been posited to reflect the post-decisional evidence accumulation process that is sensitive to decision accuracy, decision confidence, and subsequent adaptation in behavior [11]. It has a highly robust association with error detection [23] that varies with the level of confidence that an error has been made, with a higher Pe amplitude reflecting greater certainty [24]. A meta-analysis found no significant association between age and the Pe, except for a group comparison between younger and older adolescents, suggesting an alteration in the Pe may arise at or before the onset of OCD symptoms and correlate with symptom onset age [25].

An increased Pe amplitude was reported in a meta-analysis of eight studies of individuals with OCD or obsessive–compulsive symptoms using choice reaction time tasks eliciting response conflict [8, 26–28]. Of the seven studies in the meta-analysis examining the Pe in adults with OCD, one found a diminished Pe and another an augmented Pe in OCD cases compared to HC [8, 27, 28]. The only study in the meta-analysis with younger participants found significant associations between higher ERN and Pe amplitudes and parent-reported obsessive–compulsive behaviors in a non-clinical sample of 10-year-old children [26]. However, no studies have examined the Pe and Pc in pediatric OCD [8].

The following study was done with 105 older children and adolescents with a lifetime diagnosis of OCD and 105 age- and sex-matched healthy controls (HC) using a flanker task [20–22]. The first aim was to compare ERN and Pe measures and flanker task accuracy in OCD cases and HC. The second aim was to compare those measures in TR OCD cases, NTR OCD cases, and HC, because previous studies lacked adequate statistical power to assess them in the two OCD subtypes [8, 20, 29]. The third aim was to compare those measures in current OCD cases, past OCD cases, and HC, because studies have suggested the ERN is a state-independent measure but have not examined that aspect of the Pe [15, 17–19]. As the largest group differences in the brain potentials were found with the ERN and ΔPe, those measures were used in subsequent analyses. The fourth aim was to do a multiple regression analysis in all participants to examine the association of flanker task accuracy with age, lifetime OCD diagnosis, ERN, and ΔPe. The fifth aim was to do separate multiple regression analyses in all participants to examine the association of the ERN and ΔPe with age, flanker task accuracy, lifetime OCD diagnosis, and Child Behavior Checklist/6–18 (CBCL/6–18) *DSM*-Oriented Scale scores and determine whether a dimensional measure of clinical symptoms may have a stronger association with either brain potential than a lifetime OCD diagnosis [30, 31]. The sixth aim was to do a multiple regression analysis in OCD cases alone to examine the association of age at OCD symptom onset with age, lifetime tic disorder diagnosis, ERN, and ΔPe. Because the ERN and Pe have different developmental trajectories, it was hypothesized the ΔPe may be more strongly associated than the ERN with OCD symptom onset age (16, 25).

Methods

Participants

Patients with OCD were recruited from the Department of Psychiatry at the University of Michigan and surrounding community. HC were recruited from the surrounding community and were matched to patients by age and sex. Participants were recruited using flyers and UM Health Research Studies (http://www.UMHealthResearch.org). Participants or their parents gave written informed consent in accordance with the Declaration of Helsinki. All tasks and procedures were approved by the University of Michigan Medical School Institutional Review Board. Participants were paid for their interviews and psychophysiological recordings. Participants were excluded if they made fewer than 10 errors (n = 8), leaving a total of 210 participants. The final sample consisted of 80 males and 130 females of age 8–18 years, with an ethnic/racial breakdown that was 89% Caucasian, 1% African American, 3% Latino, 3% Asian, and 4% Native American. The case and control groups each had 40 males and 65 females. Female participants were significantly older than male participants (t (208) = 3.86, P = 0.0002). All participants lived with at least one English-speaking biological parent willing to participate in the research. Tables 1, 2, and 3 summarize the demographic, clinical, behavioral, and ERP data for the participants.

Table 1 Demographic, clinical, behavioral, and brain potential data in patients with OCD and healthy controls

Variable	Patients with OCD (n = 105)		Healthy Controls (n = 105)		Patients with OCD vs. Healthy Controls	
	Mean	SD	Mean	SD	Test Statistic	*P*
Demographic and Clinical Data						
Age (year)	13.6	3.0	13.7	2.0	$t_{208} = 0.05$	0.96
Age at onset of OCD symptoms (year)	7.8	3.2				
Duration of OCD symptoms (year)	5.7	3.7				
CY-BOCS lifetime score	27.0	6.9				
CY-BOCS current score	16.4	8.9				
Child Behavior Checklist/6–18						
Obsessive–Compulsive Problems	6.3	3.7	1.0	1.1	$t_{207} = 14.01$	< 0.0001
Total Problems	36.4	22.6	9.2	8.9	$t_{207} = 11.48$	< 0.0001
Internalizing Problems	14.3	9.3	3.0	3.1	$t_{207} = 11.83$	< 0.0001
Externalizing Problems	6.8	6.7	2.3	3.3	$t_{207} = 6.15$	< 0.0001
Affective Problems	4.4	3.7	0.7	1.3	$t_{207} = 9.68$	< 0.0001
Anxiety Problems	4.4	2.9	0.7	1.2	$t_{207} = 12.01$	< 0.0001
Somatic Problems	2.2	2.4	0.5	1.0	$t_{207} = 6.77$	< 0.0001
Attention Deficit/Hyperactivity Problems	3.2	3.3	1.3	1.9	$t_{207} = 5.09$	< 0.0001
Oppositional Defiant Problems	2.4	2.3	1.1	1.6	$t_{207} = 4.47$	< 0.0001
Conduct Problems	1.4	2.3	0.5	1.0	$t_{207} = 3.63$	0.0004
Behavioral Data						
Total number of trials	470.4	66.6	475.0	65.7	$t_{208} = 0.51$	0.61
Total number of error trials	51.5	30.5	42.1	22.6	$t_{208} = 2.53$	0.01
Accuracy on all trials	0.88	0.07	0.91	0.05	$t_{208} = 2.97$	0.003
Accuracy on congruent trials	0.95	0.05	0.97	0.03	$t_{208} = 2.34$	0.02
Accuracy on incongruent trials	0.81	0.10	0.84	0.07	$t_{208} = 2.89$	0.004
Accuracy after correct trials	0.88	0.07	0.91	0.05	$t_{208} = 2.80$	0.006
Accuracy after incorrect trials	0.87	0.10	0.91	0.07	$t_{208} = 3.03$	0.003
Error trial reaction time (ms)	475.3	254.6	457.4	184.1	$t_{208} = 0.58$	0.56
Correct trial reaction time (ms)	511.1	172.9	504.1	137.1	$t_{208} = 0.32$	0.75
Reaction time after error trials (ms)	507.8	186.4	501.4	141.6	$t_{208} = 0.28$	0.78
Reaction time after correct trials (ms)	504.1	176.1	497.6	139.4	$t_{208} = 0.31$	0.76
Post-error slowing (ms)	37.7	84.3	46.6	68.6	$t_{208} = 0.84$	0.40
Event-Related Brain Potential Data						
Error-related negativity, Cz (μV)	−1.63	5.88	1.44	5.93	$F_{1, 206} = 19.36$	< 0.0001
Correct-response negativity, Cz (μV)	3.19	5.07	4.35	4.65	$F_{1, 206} = 5.58$	0.02
ΔERN, Cz (μV)	−4.82	6.20	−2.91	6.06	$F_{1, 206} = 6.19$	0.01
ERN standardized residual scores, Cz (μV)	−1.26	5.48	1.26	5.52	$F_{1, 206} = 14.65$	0.0002
CRN standardized residual scores, Cz (μV)	−0.11	4.72	0.11	4.33	$F_{1, 206} = 0.61$	0.44
Error positivity, CPz (μV)	10.12	8.53	12.64	9.90	$F_{1, 206} = 2.19$	0.14
Correct positivity, CPz (μV)	−3.42	7.68	−5.83	7.19	$F_{1, 206} = 4.03$	0.046
ΔPe, CPz (μV)	13.54	9.30	18.47	9.30	$F_{1, 206} = 9.88$	0.002
Pe standardized residual scores, CPz (μV)	−1.80	8.02	1.80	8.94	$F_{1, 206} = 5.91$	0.02
Pc standardized residual scores, CPz (μV)	1.57	7.21	−1.57	6.45	$F_{1, 206} = 7.85$	0.006

The Child Behavior Checklist/6–18 was not completed for one patient with OCD at the time of event-related potential data collection

OCD obsessive–compulsive disorder, *CY-BOCS* Children's Yale-Brown Obsessive Compulsive Scale, *ERN* error-related negativity, *CRN* correct-response negativity, *ΔERN* error-related negativity minus correct-response negativity, *Pe* error positivity, *Pc* correct positivity, *ΔPe* error positivity minus correct positivity, *SD* standard deviation

Table 2 Demographic, clinical, behavioral, and brain potential data in patients with tic-related OCD, patients with non-tic-related OCD, and healthy controls

Variable	Patients with TR OCD (n = 21)		Patients with NTR OCD (n = 84)		Healthy Controls (n = 105)		Patients with TR OCD vs. Patients with NTR OCD vs. Healthy Controls	
	Mean	SD	Mean	SD	Mean	SD	Test Statistic	*P*
Demographic and Clinical Data								
Age (year)	12.3	3.1	14.0	2.8	13.6	3.0	$F_{2, 207} = 2.82$	0.06
Sex (male/female)	11/10		29/55		40/65		$\chi^2_2 = 2.27$	0.32
Age at onset of OCD symptoms (year)	6.0	3.0	8.3	3.1			$t_{103} = 3.11$	0.002
Duration of OCD symptoms (year)	6.0	3.2	5.5	3.8			$t_{103} = 0.56$	0.58
SSRI (treatment/no treatment)	7/14		36/48				$\chi^2_1 = 0.63$	0.43
CY-BOCS lifetime score	30.1	6.2	26.2	6.9			$t_{103} = 2.37$	0.02
CY-BOCS current score	21.7	7.4	15.0	8.8			$t_{103} = 3.15$	0.002
Behavioral Data								
Total number of trials	449.6	101.5	475.6	54.2	475.0	65.7	$F_{2, 206} = 1.44$	0.24
Total number of error trials	51.6	28.7	51.5	31.0*	42.1	22.6	$F_{2, 206} = 3.20$	0.04
Accuracy on all trials	0.88	0.06*	0.88	0.07**	0.91	0.05	$F_{2, 206} = 4.48$	0.01
Accuracy on congruent trials	0.95	0.03	0.96	0.05	0.97	0.03	$F_{2, 206} = 2.86$	0.06
Accuracy on incongruent trials	0.80	0.11	0.81	0.10**	0.84	0.07	$F_{2, 206} = 4.20$	0.02
Accuracy after correct trials	0.88	0.06	0.88	0.07**	0.91	0.05	$F_{2, 206} = 3.90$	0.02
Accuracy after incorrect trials	0.84	0.09***	0.88	0.10*	0.91	0.07	$F_{2, 206} = 6.57$	0.002
Error reaction time (ms)	544.1	309.2	458.1	238.0	457.5	184.0	$F_{2, 206} = 1.44$	0.24
Correct reaction time (ms)	577.0	197.8	494.6	163.3	504.1	137.1	$F_{2, 206} = 2.44$	0.09
Reaction time after error trials (ms)	559.9	218.0	494.8	176.5	501.4	141.6	$F_{2, 206} = 1.35$	0.26
Reaction time after correct trials (ms)	569.9	199.6	487.7	167.0	497.6	139.4	$F_{2, 206} = 2.33$	0.10
Post-error slowing (ms)	15.5	106.6	43.2	77.6	46.6	68.6	$F_{2, 206} = 1.45$	0.24
Event-Related Brain Potential Data								
Error-related negativity, Cz (μV)	−1.45	6.39*	−1.68	5.79****	1.44	5.93	$F_{2, 205} = 9.70$	< 0.0001
Correct response negativity, Cz (μV)	3.46	5.21	3.12	5.07*	4.35	4.65	$F_{2, 205} = 3.20$	0.04
ΔERN, Cz (μV)	−4.91	6.52*	−4.80	6.15*	−2.91	6.06	$F_{2, 205} = 3.69$	0.03
ERN standardized residual scores, Cz (μV)	−1.21	5.91*	−1.27	5.40***	1.26	5.52	$F_{2, 205} = 7.60$	0.0007
CRN standardized residual scores, Cz (μV)	0.11	4.82	−0.16	4.72	0.11	4.33	$F_{2, 205} = 0.95$	0.39
Error positivity, CPz (μV)	9.67	9.81	10.23	8.24	12.64	9.90	$F_{2, 205} = 1.12$	0.33

Table 2 (continued)

Variable	Patients with TR OCD (n = 21)		Patients with NTR OCD (n = 84)		Healthy Controls (n = 105)		Patients with TR OCD vs. Patients with NTR OCD vs. Healthy Controls	
	Mean	SD	Mean	SD	Mean	SD	Test Statistic	*P*
Correct positivity, CPz (μV)	−3.58	8.47	−3.38	7.52	−5.83	7.19	$F_{2, 205} = 2.01$	0.14
ΔPe, CPz (μV)	13.25	9.04*	13.61	9.41**	18.47	9.30	$F_{2, 205} = 4.99$	0.008
Pe standardized residual scores, CPz (μV)	−2.18	8.48	−1.71	7.95*	1.80	8.94	$F_{2, 205} = 3.00$	0.05
Pc standardized residual scores, CPz (μV)	1.54	7.40	1.58	7.21*	−1.57	6.45	$F_{2, 205} = 3.94$	0.02

The Child Behavior Checklist was not completed for one patient with obsessive–compulsive disorder at the time of event-related potential data collection

OCD obsessive–compulsive disorder, *TR* tic-related, *NTR* non-tic-related, *CY-BOCS* Children's Yale-Brown Obsessive Compulsive Scale, *ERN* error-related negativity, *CRN* correct-response negativity, *ΔERN* error-related negativity minus correct-response negativity, *Pe* error positivity, *Pc* correct positivity, *ΔPe* error positivity minus correct positivity, *SD* standard deviation

*Compared to healthy controls, $P < 0.05$; ** compared to healthy controls, $P < 0.01$; *** compared to healthy controls, $P < 0.001$; **** compared to healthy controls, $P < 0.0001$

All 105 patients had a lifetime diagnosis of OCD, with 76 having a current diagnosis and 29 a past diagnosis with OCD symptoms that no longer met criteria for diagnosis. Twenty-one patients had a lifetime diagnosis of a tic disorder. Patients were excluded if they had a lifetime diagnosis of autism spectrum disorder, anorexia nervosa, schizophrenia, other psychotic disorder, bipolar disorder, or substance-related disorder. The 105 HC had no history of a specific axis I disorder. Lifetime and current axis I diagnoses were made independently by two clinicians using all sources of information according to *DSM-5* criteria [32]. Participants were excluded if they had a history of intellectual disability, head injury with a loss of consciousness, chronic neurological disorder other than tics, or scores higher than 14 on the Social Communication Questionnaire [33]. Because studies have indicated that treatment with a serotonin reuptake inhibitor (SRI) has no effect on the ERN, 43 patients were enrolled taking a stable dose of an SRI but no other medications [15, 17–19, 27]. Medicated patients were significantly older than unmedicated patients ($t(103) = 2.72$, $P = 0.008$).

Diagnostic Instruments

All 210 participants were interviewed with the Schedule for Schizophrenia and Affective Disorders for School-Aged Children-Present and Lifetime Version and Schedule for Obsessive–Compulsive and Other Behavioral Syndromes [34, 35]. The maximum and current severity of OCD symptoms in patients was assessed with a modified version of the Children's Yale-Brown Obsessive Compulsive Disorder Scale [36]. Parents completed the CBCL/6–18 and SCQ about their children [30, 31, 33].

Stimulus Material and Task Procedures

Participants performed a modified Eriksen flanker task in which arrows appeared on a computer display with congruent (e.g., → → → → →) and incongruent (e.g., → → ← → →) conditions [37]. They were instructed to respond by pressing one of two buttons indicating the direction of the central arrow (i.e., right versus left), while ignoring the adjacent arrows, and to respond as quickly and accurately as possible, placing equal emphasis on speed and accuracy (20–22). The flanker task is a test of selective attention and response inhibition that activates the anterior cingulate cortex and pre-supplementary motor cortex [38] and provides a more efficient and reliable measure of ERN amplitude than the Stroop or Go/NoGo tasks [15, 38]. The stimuli remained on the screen for 250 ms, with an interval of 1500 ms between consecutive trials. Each participant was seated 0.65 m directly in front of the computer monitor. Following 40 practice trials, each subject completed 8 blocks of 64 trials with the number of completed trials ranging from 256 to 512. Performance feedback was provided after every block to yield an error rate of approximately 10%, with encouragement to focus on speed if there were fewer than four errors or to focus on accuracy if there were more than 10 errors [20–22].

Table 3 Demographic, clinical, behavioral, and brain potential data in patients with current OCD, patients with past OCD, and healthy controls

Variable	Current OCD Patients (n = 76)		Past OCD Patients (n = 29)		Healthy Controls (n = 105)		Current OCD Patients vs. Past OCD Patients vs. Healthy Controls	
	Mean	SD	Mean	SD	Mean	SD	Test Statistic	*P*
Demographic and Clinical Data								
Age (year)	13.4	2.9	14.3	2.8	13.6	3.0	$F_{2, 207} = 1.13$	0.32
Sex (male/female)	29/47		11/18		40/65		$\chi^2_2 = 0.00$	0.999
Age at onset of OCD symptoms (year)	7.4	3.1	8.9	3.2			$t_{103} = 2.22$	0.03
Duration of OCD symptoms (year)	5.8	0.4	4.8	0.7			$t_{103} = 1.23$	0.22
CY-BOCS lifetime score	27.4	6.9	25.9	6.9			$t_{103} = 1.02$	0.31
CY-BOCS current score	19.8	7.5	7.2	4.8			$t_{103} = 8.37$	< 0.0001
SSRI (treatment/no treatment)	28/48		15/14				$\chi^2_1 = 1.92$	0.17
Behavioral Data								
Total number of trials	468.6	71.0	475.1	54.2	475.0	65.7	$F_{2, 206} = 0.14$	0.87
Total number of error trials	50.1	32.3	55.1	25.1**	42.1	22.6	$F_{2, 206} = 3.65$	0.03
Accuracy on all trials	0.88	0.07*	0.87	0.06**	0.91	0.05	$F_{2, 206} = 5.17$	0.006
Accuracy on congruent trials	0.95	0.05*	0.96	0.03	0.97	0.03	$F_{2, 206} = 2.99$	0.05
Accuracy on incongruent trials	0.81	0.11*	0.78	0.10***	0.84	0.07	$F_{2, 206} = 5.62$	0.004
Accuracy after correct trials	0.89	0.07*	0.87	0.06**	0.91	0.05	$F_{2, 206} = 4.88$	0.008
Accuracy after incorrect trials	0.87	0.11**	0.88	0.10**	0.91	0.07	$F_{2, 206} = 4.72$	0.01
Error reaction time (ms)	501.5	280.9	406.7	150.6	457.5	184.0	$F_{2, 206} = 1.22$	0.30
Correct reaction times (ms)	533.8	188.0	451.4	106.1	504.1	137.1	$F_{2, 206} = 1.91$	0.15
Reaction time after error trials (ms)	529.9	200.5	449.8	127.7	501.4	501.4	$F_{2, 206} = 1.50$	0.23
Reaction time after correct trials (ms)	526.8	190.9	444.7	167.0	497.6	139.4	$F_{2, 206} = 1.79$	0.17
Post-error slowing (ms)	34.2	95.1	46.8	45.8	46.6	68.6	$F_{2, 206} = 0.46$	0.63
Event-Related Brain Potential Data								
Error-related negativity, Cz (μV)	−1.54	6.04****	−1.87	5.54**	1.44	5.93	$F_{2, 205} = 9.64$	< 0.0001
Correct response negativity, Cz (μV)	3.09	4.87	3.47	5.66	4.35	4.65	$F_{2, 205} = 2.81$	0.06
ΔERN, Cz (μV)	−4.62	6.17*	−5.32	6.34	−2.91	6.06	$F_{2, 205} = 3.69$	0.048
ERN standardized residual scores, Cz (μV)	−1.12	5.60****	−1.63	5.22*	1.26	5.52	$F_{2, 205} = 7.29$	0.0009
CRN standardized residual scores, Cz (μV)	−0.24	4.51	0.23	5.29	0.11	4.33	$F_{2, 205} = 0.32$	0.72
Error positivity, CPz (μV)	10.41	8.29	9.35	9.24	12.64	9.90	$F_{2, 205} = 1.15$	0.32
Correct positivity, CPz (μV)	−3.20	7.21	−3.99	8.90	−5.83	7.19	$F_{2, 205} = 2.31$	0.10
ΔPe, CPz (μV)	13.61	9.20**	13.34	9.71	18.47	9.30	$F_{2, 205} = 4.95$	0.008
Pe standardized residual scores, CPz (μV)	−1.61	7.94	−2.31	8.35	1.80	8.94	$F_{2, 205} = 2.94$	0.06

Table 3 (continued)

Variable	Current OCD Patients (n = 76)		Past OCD Patients (n = 29)		Healthy Controls (n = 105)		Current OCD Patients vs. Past OCD Patients vs. Healthy Controls	
	Mean	SD	Mean	SD	Mean	SD	Test Statistic	*P*
Pc standardized residual scores, CPz (μV)	1.72	6.88**	1.23	8.12	−1.57	6.45	$F_{2, 205} = 4.17$	0.02

The Child Behavior Checklist was not completed for one patient with obsessive–compulsive disorder at the time of event-related potential data collection

OCD obsessive–compulsive disorder, *CY-BOCS* Children's Yale-Brown Obsessive Compulsive Scale, *ERN* error-related negativity, *CRN* correct-response negativity, *ΔERN* error-related negativity minus correct-response negativity, *Pe* error positivity, *Pc* correct positivity, *ΔPe* error positivity minus correct positivity, *SD* standard deviation

*Compared to healthy controls, $P < 0.05$; ** compared to healthy controls, $P < 0.01$; *** compared to healthy controls, $P < 0.001$; **** compared to healthy controls, $P < 0.0001$

Electrophysiological Recording and Data Reduction

The electroencephalogram was recorded from DC-104 Hz with 64 Ag/AgCl scalp electrodes, two mastoid electrodes, and two vertical and two horizontal electro-oculogram electrodes, using the BioSemi ActiveTwo system (Amsterdam, the Netherlands). Data were digitized at 512 Hz, referenced to a ground formed from a common mode sense active electrode and driven right leg passive electrode (see http://www.biosemi.com/faq/cms&drl.htm), and rereferenced offline to the average of the two mastoid electrodes. Data were band-pass filtered 0.1–30 Hz using zero-phase shift filters. EEG data were screened using automated algorithms that rejected epochs in which absolute voltage exceeded 500 μV and epochs containing peak to peak activity > 500 μV within 200 ms, with a 100 ms moving window, for midline channels (Fz, FCz, Cz, CPz, Pz). Ocular movement artifacts were then corrected using a regression-based algorithm [40]. After ocular correction, individual trials were rejected if they contained absolute amplitudes > 100 μV, a change > 50 μV measured from one data point to the next point, or a maximum voltage difference < 0.5 μV within a trial in any of the midline electrodes.

The mean amplitude of the ERN was computed on error trials in a window from 0 to 80 ms following the incorrect response, relative to a pre-response baseline of – 200 to – 50 ms. The mean amplitude of the Pe was computed on error trials in a window from 200 to 400 ms following the erroneous response, compared to a pre-response baseline of – 200 to – 50 ms. The CRN and Pc consisted of the same respective measures computed on correct trials. Amplitudes were calculated for electrodes Fz, FCz, Cz, CPz, and Pz, with the focus of the present study on the ERN measures at Cz and the Pe measures at CPz. Correlational analyses with the ERN and CRN indicate that numerically greater negative values represent higher ERP amplitudes, whereas correlational analyses with the Pe and Pc indicate that numerically greater positive values represent higher ERP amplitudes.

The ΔERN was calculated by subtracting the CRN from the ERN, since it may isolate neural activity unique to error processing from activity more broadly related to response monitoring [7]. The ΔERN is correlated both with the ERN and CRN and is therefore not an independent measure of either ERP [41]. ERN and CRN standardized residual scores (ERN_{resid} and CRN_{resid}) were calculated based on measuring the variance leftover in a regression equation in which one score is modeled as a predictor of another score, because they may be preferable to subtraction-based difference scores in separating error processing from response monitoring [22, 41]. Similar measures were calculated for the ΔPe, Pe_{resid}, and Pc_{resid}.

Behavioral measures included the number of erroneous and correct trials for each subject, as well as accuracy expressed as a percentage of valid trials. Mean reaction times on error and correct trials were calculated separately, and trials were excluded if their reaction times were > 3 standard deviations from the mean. Reaction time and accuracy after errors were evaluated to determine whether there were group differences in post-error behavioral adjustments [7]. Reaction times were analyzed with group as a between-subject factor and response type as a within-subject factor. The mean number of errors per subject contributing to the analysis was 46.8 (SD = 27.2; range = 10–160).

Statistical Analyses

Student *t* tests, χ^2, analysis of variance, and analysis of covariance tests were used to evaluate group differences in demographic, clinical, and behavioral data. Pearson correlation coefficients were used to examine associations of response-related amplitudes with age, behavioral measures, and clinical measures. Ten electrocortical indicators (ERN, CRN, ΔERN, ERN_{resid}, CRN_{resid}, Pe, Pc, ΔPe, Pe_{resid} and Pc_{resid}) of performance monitoring were

analyzed separately using a repeated-measure analysis of covariance with group (OCD cases and HC) as a between-subject factor, response type (correct and error) as a within-subject factor, and age and accuracy as covariates [7]. Similar analyses were done to compare brain potentials in male and female participants, TR and NTR OCD cases, cases with a current or past OCD diagnosis, and medicated and unmedicated OCD cases. Cohen's effect size conventions were used to describe the magnitude of effects (small: $d \geq 0.20$; medium: $d \geq 0.50$; large: $d \geq 0.80$) [42].

A multiple linear regression analysis was done with all participants to examine the association of flanker task accuracy with age, lifetime OCD diagnosis, ERN, and ΔPe. Separate multiple linear regression analyses were done with all participants to examine the relation of the ERN and ΔPe to age, flanker task accuracy, lifetime OCD diagnosis, and CBCL/6–18 *DSM*-Oriented Scale scores (obsessive compulsive, affective, anxiety, somatic, attention deficit/hyperactivity, oppositional defiant, and conduct problems) [30, 31]. A multiple regression analysis was done with OCD cases alone to examine the association of age at OCD symptom onset with age, lifetime tic disorder diagnosis, ERN, and ΔPe. Analyses were performed with JMP Pro Version 14 software. All tests were two-tailed with $\alpha = 0.05$.

Results

Behavioral Data in Patients with OCD and Healthy Controls

Participants had significantly higher flanker task accuracy on congruent than incongruent trials (paired t (209) = 26.42, $P < 0.0001$). OCD cases were significantly less accurate than HC in all trial conditions (all P values < 0.05) (Table 1). Compared to HC, overall accuracy was also significantly decreased in TR and NTR OCD cases (both P values < 0.05) (Table 2) and current and past OCD cases (both P values < 0.05) (Table 3).

Correct responses were significantly slower than incorrect responses (paired t (209) = 6.33, $P < 0.0001$). No main effect of group or response type for reaction time and no interaction between group and response type for reaction time reached significance ($P = 0.63$ and $P = 0.40$, respectively). Age had significant positive correlations with accuracy ($r = 0.17$, $P = 0.01$), post-correct accuracy ($r = 0.16$, $P = 0.02$), and post-error accuracy ($r = 0.21$, $P = 0.002$). Age had significant negative correlations with reaction time on correct ($r = -0.57$, $P < 0.0001$) and incorrect trials ($r = -0.46$, $P < 0.0001$) and a significant positive correlation with post-error slowing ($r = 0.21$, $P = 0.002$).

There were no significant sex differences in flanker task accuracy, reaction time on correct or incorrect trials, or post-error slowing (all P values > 0.5). There were no significant differences in accuracy, reaction time on correct or error trials, or post-error slowing between medicated and unmedicated OCD cases (all P values > 0.1), TR and NTR OCD cases (all P values > 0.37) (Table 2), and current and past OCD cases (all P values > 0.09) (Table 3).

Event-Related Potential Data in Patients with OCD and Healthy Controls

ERN amplitude was significantly increased (more negative) compared to CRN amplitude (paired t (209) = – 9.05, $P < 0.0001$), and Pe amplitude was significantly increased (more positive) compared to Pc amplitude (paired t (209) = 24.16, $P < 0.0001$). Age in all participants had significant correlations with the ERN ($r = -0.20$, $P = 0.004$), CRN ($r = 0.24$, $P = 0.0005$), and ΔERN ($r = -0.38$, $P < 0.0001$) but not Pe, Pc, or ΔPe (all P values > 0.14). Accuracy had significant correlations with the ERN ($r = -0.17$, $P = 0.02$) but not CRN or ΔERN (both P values > 0.07). Accuracy also had significant correlations with the Pe ($r = 0.18$, $P = 0.009$) and ΔPe ($r = 0.26$, $P = 0.0001$) but not Pc ($P = 0.10$). Supplementary Table 1 provides a correlation matrix for age, flanker task accuracy, and the ten brain potentials.

ERN amplitude was significantly increased in OCD cases compared to HC ($F_{1, 206} = 19.36$, $P < 0.0001$, Cohen's $d = 0.52$), with significant effects for accuracy ($F_{1, 206} = 7.55$, $P = 0.006$) and age ($F_{1, 206} = 6.63$, $P = 0.01$) (Table 1; Fig. 1). CRN amplitude was significantly enlarged in cases compared to HC ($F_{1, 206} = 5.58$, $P = 0.02$, Cohen's $d = 0.24$), with significant effects for accuracy ($F_{1, 206} = 8.73$, $P = 0.004$) and age ($F_{1, 206} = 16.55$, $P < 0.0001$). The ΔERN was significantly enhanced in cases compared to HC ($F_{1, 206} = 6.19$, $P = 0.014$, Cohen's $d = 0.31$), with a significant effect for age ($F_{1, 206} = 35.16$, $P < 0.0001$) but not accuracy ($P = 0.73$).

There was no significant group difference in Pe amplitude ($P = 0.14$) (Table 1; Fig. 1). Pc amplitude was significantly increased in OCD cases compared to HC ($F_{1, 206} = 4.02$, $P = 0.046$, Cohen's $d = 0.32$), without significant effects for accuracy or age (both P values > 0.08). Moreover, the ΔPe was significantly decreased in cases compared to controls ($F_{1, 206} = 9.88$, $P = 0.002$, Cohen's $d = 0.53$), with a significant effect for accuracy ($F_{1, 206} = 12.76$, $P = 0.002$) but not age ($P = 0.07$).

Results for the ERN_{resid}, CRN_{resid}, Pe_{resid}, and Pc_{resid} in these two groups are summarized in Table 1. There were no significant sex differences in any brain potentials (all P values > 0.05). There were no significant differences in any brain potentials between medicated and unmedicated OCD cases (all P values > 0.10), TR OCD and NTR OCD cases

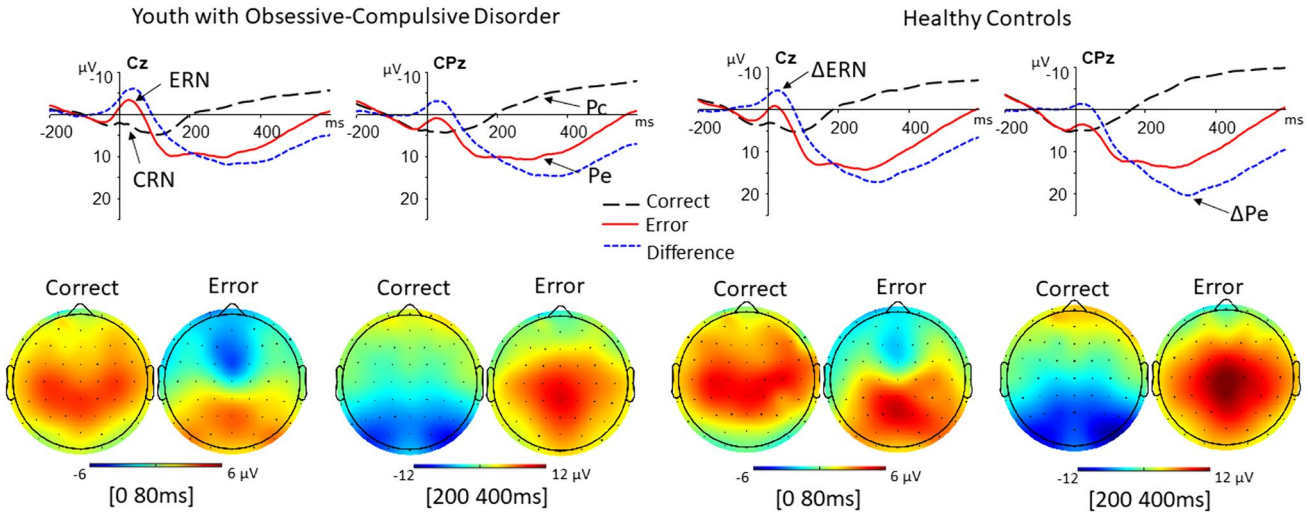

Fig. 1 Grand averages of electroencephalogram (EEG) recordings in 105 patients with obsessive–compulsive disorder (OCD) and 105 healthy controls (HC). Note: The top images depict response-locked grand average waveforms recorded at the Cz and CPz electrodes for correct and incorrect responses. Responses occurred at 0 ms. The mean amplitude of the error-related negativity (ERN) was computed in a window 0–80 ms after incorrect response trials. The mean amplitude of the correct response negativity (CRN) consisted of the same measure computed on correct response trials. The ΔERN was calculated by subtracting the CRN from the ERN. The mean amplitude of the error positivity (Pe) was computed in a window 200–400 ms after incorrect response trials. The mean amplitude of the correct positivity (Pc) consisted of the same measure computed on correct response trials. The ΔPe was calculated by subtracting the Pc from the Pe. The bottom images depict the topography of mean amplitudes of erroneous and correct waveforms measured between 0 and 80 ms and between 200 and 400 ms

(all P values > 0.35) (Table 2), and current and past OCD cases (all P values > 0.55) (Table 3).

Event-Related Potential Data in Patients with TR OCD, Patients with NTR OCD, and Healthy Controls

In a comparison of the ERN in TR OCD cases, NTR OCD cases, and HC, there were significant effects for group ($F_{2, 205} = 9.70$, $P < 0.0001$), age ($F_{1, 205} = 6.72$, $P = 0.01$), and accuracy ($F_{1, 205} = 7.52$, $P = 0.007$) (Table 2). ERN amplitude was significantly increased in TR OCD cases compared to HC ($F_{1, 122} = 6.09$, $P = 0.02$), without significant effects for age or accuracy (both P values > 0.07). ERN amplitude was also significantly enlarged in NTR OCD cases compared to HC ($F_{1, 185} = 16.72$, $P < 0.0001$), with significant effects for age ($F_{1, 185} = 8.44$, $P = 0.004$) and accuracy ($F_{1, 185} = 7.65$, $P = 0.006$).

In a comparison of the ΔPe in TR OCD cases, NTR OCD cases, and HC, there were significant effects for group ($F_{2, 205} = 4.99$, $P = 0.008$) and accuracy ($F_{2, 205} = 12.72$, $P = 0.0005$) but not age ($P = 0.06$) (Table 2). The ΔPe was significantly decreased in TR OCD cases compared to HC ($F_{1, 122} = 4.43$, $P = 0.04$), with significant effects for accuracy ($F_{1, 122} = 8.02$, $P = 0.005$) and age ($F_{1, 122} = 4.14$, $P = 0.04$). The ΔPe was also significantly diminished in NTR OCD cases compared to HC ($F_{1, 185} = 7.73$, $P = 0.006$), with a significant effect for accuracy ($F_{1, 185} = 13.80$, $P = 0.0003$) but not age ($P = 0.77$). Results for the CRN, ΔERN, ERN_{resid}, CRN_{resid}, Pe, Pc, Pe_{resid}, and Pc_{resid} in these three groups are summarized in Table 2.

Event-Related Potential Data in Patients with Current OCD, Patients with Past OCD, and Healthy Controls

In a comparison of the ERN in current OCD cases, past OCD cases, and HC, there were significant effects for group ($F_{2, 205} = 9.64$, $P < 0.0001$), age ($F_{1, 205} = 6.42$, $P = 0.01$), and accuracy ($F_{1, 205} = 7.54$, $P = 0.007$) (Table 3). ERN amplitude was significantly increased in current OCD cases compared to HC ($F_{1, 177} = 16.02$, $P < 0.0001$), with significant effects for age ($F_{1, 177} = 8.44$, $P = 0.02$) and accuracy ($F_{1, 177} = 7.67$, $P = 0.006$). ERN amplitude was also significantly enlarged in past OCD cases compared to HC ($F_{1, 130} = 6.99$, $P = 0.009$), with a significant effect for age ($F_{1, 130} = 5.11$, $P = 0.02$) but not accuracy ($P = 0.39$).

In a comparison of the ΔPe in current OCD cases, past OCD cases, and HC, there were significant effects for group ($F_{2, 205} = 4.95$, $P = 0.008$) and accuracy ($F_{2, 205} = 12.78$, $P = 0.0004$) but not age ($P = 0.06$) (Table 3). The ΔPe was significantly decreased in current OCD cases compared to HC ($F_{1, 177} = 9.54$, $P = 0.002$), with a significant effect for accuracy ($F_{1, 177} = 7.42$, $P = 0.007$) but not age ($P = 0.09$). There was no significant ΔPe difference between past OCD

cases and HC ($P = 0.17$). Results for the CRN, ΔERN, ERN_{resid}, CRN_{resid}, Pe, Pc, Pe_{resid}, and Pc_{resid} in these three groups are summarized in Table 3.

Flanker Task Accuracy and Event-Related Potential Data in Patients with OCD and Healthy Controls

Because of the group differences in the ERN and ΔPe noted above along with the strong correlation of accuracy with age, a multiple linear regression analysis was done using age, lifetime OCD diagnosis, and both brain potentials as predictors to determine their associations with flanker task accuracy as the dependent variable. Age, lifetime OCD diagnosis, and both brain potentials were significantly associated with flanker task accuracy in all participants, with a more negative ERN and more positive ΔPe associated with higher accuracy (Supplementary Table 2).

Clinical and Event-Related Potential Data in Patients with OCD and HC

Separate multiple linear regression analyses were done with all participants with either the ERN or ΔPe as the dependent variable and age, flanker task accuracy, lifetime OCD diagnosis, and CBCL/6–18 *DSM*-Oriented Scale scores as predictors. The ERN had significant associations with CBCL/6–18 Anxiety Problems Scale scores, age, and accuracy in the full model (Table 4). Backward stepwise regression analysis determined that only Anxiety Problems Scale scores and age were significantly associated with the ERN in the reduced model. The ERN had a significant negative correlation with Anxiety Problems Scale scores in OCD cases ($r = -0.30$, $P = 0.002$) but not HC ($P = 0.46$).

The ΔPe had significant associations with accuracy and age in the full model (Table 5). Backward stepwise regression analysis found that accuracy, CBCL/6–18 Obsessive Compulsive Problems Scale scores, and age were significantly associated with the ΔPe in the reduced model. The ΔPe had no significant correlations with Obsessive Compulsive Problems Scale scores in either OCD cases or HC alone (both P values > 0.18). Supplementary Table 3 provides a correlation matrix for the ten brain potentials and seven CBCL/6–18 *DSM*-Oriented Scales.

Age at OCD Symptom Onset and Event-Related Potential Data in Patients with OCD

A multiple linear regression analysis was done with OCD cases to examine the relation of age, lifetime tic disorder diagnosis, ERN, and ΔPe to age at OCD symptom onset.

Table 4 Multiple linear regression model for error-related negativity (ERN) at electrode Cz as dependent variable and age, flanker task accuracy, lifetime diagnosis of obsessive–compulsive disorder, and Child Behavior Checklist/6–18 (CBCL) *DSM*-Oriented Scales as predictors in patients with OCD and healthy controls

Full model	Regression						Correlation	
	R^2	β	β (SE)	*t*	*P*	*F*	*r* (bivariate)	*r* (partial)
	0.195				< 0.0001	4.78		
CBCL Anxiety Problems		−0.77	0.29	−2.65	0.009		−0.32	−0.19
Age		−0.35	0.14	−2.41	0.02		−0.20	−0.18
Flanker task accuracy		−14.96	6.85	−2.18	0.03		−0.16	−0.15
Obsessive–Compulsive Disorder		0.92	0.58	1.59	0.11		−0.25	−0.11
CBCL AD/H Problems		0.22	0.18	1.23	0.22		−0.03	0.09
CBCL OC Problems		0.27	0.23	1.19	0.23		−0.26	0.08
CBCL Affective Problems		−0.19	0.20	−0.92	0.36		−0.27	0.06
CBCL Conduct Problems		0.15	0.30	0.49	0.62		−0.08	0.04
CBCL Somatic Problems		−0.04	0.25	−0.17	0.87		−0.20	−0.01
CBCL Oppositional Defiant Problems		0.007	0.26	0.03	0.98		−0.07	0.001
Reduced model[a]	Regression						Correlation	
	R^2	β	β (SE)	*t*	*P*	*F*	*r* (bivariate)	*r* (partial)
	0.158				< 0.0001	19.26		
CBCL Anxiety Problems		−0.72	0.13	−5.37	< 0.0001		−0.32	−0.35
Age		−0.48	0.13	−3.63	0.0004		−0.20	−0.25

A CBCL was not completed for one patient with OCD when event-related potential data were collected

OCD obsessive–compulsive disorder, *AD/H* attention-deficit/hyperactivity, *OC* obsessive compulsive, *SE* standard error

[a]After backward stepwise deletion of nonsignificant variables

Table 5 Multiple linear regression model for error positivity minus correct positivity (ΔPe) at electrode CPz as dependent variable and age, flanker task accuracy, lifetime diagnosis of obsessive–compulsive disorder, and Child Behavior Checklist/6–18 *DSM*-Oriented Scales as predictors in patients with OCD and healthy controls

Full model	Regression						Correlation	
	R^2	β	β (SE)	t	P	F	r (bivariate)	r (partial)
	0.142				0.0006	3.27		
Flanker task accuracy		41.91	11.14	3.76	0.0002		0.26	0.26
Age		−0.49	0.23	−2.11	0.04		−0.08	−0.15
CBCL OC Problems		−0.37	0.37	−1.01	0.31		−0.21	−0.07
Obsessive– Compulsive Disorder		−1.82	1.88	−0.97	0.33		−0.26	−0.07
CBCL AD/H Problems		−0.22	0.29	−0.74	0.46		−0.11	−0.06
CBCL Affective Problems		0.19	0.33	0.58	0.56		−0.16	0.04
CBCL Oppositional Defiant Problems		0.24	0.43	0.56	0.57		−0.05	0.04
CBCL Anxiety Problems		−0.14	0.47	−0.30	0.77		−0.18	−0.02
CBCL Somatic Problems		−0.11	0.41	−0.27	0.79		−0.12	−0.02
CBCL Conduct Problems		0.02	0.49	0.04	0.97		−0.06	0.002
Reduced model[a]	Regression						Correlation	
	R^2	β	β (SE)	t	P	F	r (bivariate)	r (partial)
	0.132				< 0.0001	10.41		
Flanker task accuracy		44.68	10.43	4.28	< 0.0001		0.26	0.29
CBCL OC Problems		−0.55	0.16	−3.37	0.0009		−0.21	−0.23
Age		−0.48	0.13	−2.23	0.03		−0.08	−0.15

A CBCL was not completed for one patient with OCD when event-related potential data were collected

OCD obsessive–compulsive disorder, *AD/H* attention-deficit hyperactivity, *OC* obsessive compulsive, *SE* standard error

[a]After backward stepwise deletion of nonsignificant variables

OCD symptom onset age had significant associations with age and lifetime tic disorder diagnosis in the full model (Supplementary Table 4). Backward stepwise regression analysis found that tic disorder, age, and ΔPe were significantly associated with age at OCD symptom onset in the reduced model. The ΔPe had a significant positive correlation with age at OCD symptom onset in NTR OCD cases ($r = 0.25$, $P = 0.02$) but not TR OCD cases ($P = 0.62$). ERN amplitude had no significant correlations with age at OCD symptom onset in either TR OCD or NTR OCD cases (both P values > 0.19).

Discussion

Consistent with previous reports of altered neural correlates of performance monitoring in OCD, we found an increased ERN, ΔERN, and ERN_{resid} in a large sample of children and adolescents with a history of OCD (Table 1) [7, 8, 15, 17–19]. The moderate effect size (Cohen's $d = 0.52$) for the enlarged ERN is comparable to that reported in a meta-analysis of performance monitoring studies in adults and children with OCD (Hedge's $g = 0.54$) [8]. Our finding of an increased CRN in pediatric OCD cases is consistent with several studies in adults with OCD [18, 19, 27]. We also found an increased ERN, ΔERN, and ERN_{resid} in TR and NTR OCD cases (Table 2) and an increased ERN and ERN_{resid} in current and past OCD cases (Table 3). Although an increased ERN was found in a meta-analysis of studies examining error-related brain activity in patients with either OCD or Tourette's disorder, there are no previous studies demonstrating an increased ERN in both TR and NTR OCD cases [8]. In the multiple regression analysis with the ERN as the dependent variable in the total sample, only CBCL/6–18 Anxiety Problems Scale scores and age were significant predictors in the reduced model (Table 4 and Supplementary Table 3). The ERN had a significant correlation with Anxiety Problems Scale scores in OCD cases but not HC. The results taken together support the hypothesis that an enlarged ERN is a trait-like biomarker for OCD that may also serve as a transdiagnostic biomarker for tic disorders and some anxiety disorders [8, 17–22].

In contrast to most studies of performance monitoring in OCD, we found a *decreased* ΔPe and Pe_{resid} along with an *increased* Pc and Pc_{resid} in pediatric OCD cases (Table 1) [8, 26–28]. The ΔPe was reduced in TR, NTR, and current OCD

cases but not past OCD cases (Tables 2 and 3). Further studies will be necessary to determine whether the ΔPe is a more state-like biomarker for pediatric OCD than the ERN [18, 19]. In the multiple regression analysis with the ΔPe as the dependent variable in the total sample, flanker task accuracy, CBCL/6–18 Obsessive Compulsive Problems Scale scores, and age were significant predictors in the reduced model (Table 5 and Supplementary Tables 1 and 3). In the multiple regression analysis with age at OCD symptom onset as the dependent variable in cases alone, the association between the ΔPe and OCD symptom onset age suggests an atypical development of the Pc or Pe may be involved in the pathogenesis of pediatric OCD (Supplementary Table 4). However, the correlation between the ΔPe and OCD symptom onset age was significant in the NTR OCD group but not the smaller TR OCD group.

Our ΔPe findings require replication in other large pediatric OCD samples. Studies examining the ERN and ΔPe in other psychiatric disorders may determine whether the combination of an increased ERN and a decreased ΔPe is specific to pediatric OCD. The reduced ΔPe in current but not past OCD cases and the correlations of the ΔPe with obsessive–compulsive symptom severity and OCD symptom onset age suggest that the ΔPe may be more directly involved in the pathogenesis of pediatric OCD than the ERN and that interventions augmenting the ΔPe may diminish OCD symptoms.

In contrast to studies finding normal or increased flanker task accuracy in adults with OCD, we found *decreased* flanker task accuracy in youth with OCD (Table 1) [18–20]. TR and NTR OCD cases and current and past OCD cases had similar impairments in accuracy (Tables 2 and 3). OCD cases had decreased flanker task accuracy despite having an increased ERN, suggesting that an enlarged ERN may develop over time in youth with OCD to compensate for deficits in error monitoring [42] (Supplementary Tables 1 and 2). In contrast, the correlated reductions in the ΔPe and flanker task accuracy indicate that, as the Pc and Pe become closer in amplitude, error signaling may become compromised and cause uncertainty about the correctness of a response (Supplementary Tables 1 and 2). The reduced ΔPe in pediatric OCD may reflect a defect in the post-decisional evidence accumulation process that impairs decision accuracy, decision confidence, and subsequent behavioral adjustments [11, 23, 24].

Our study has limitations requiring further consideration. Participants were primarily Caucasian and treatment was uncontrolled; however, it is doubtful that brain potentials would be different with a more diverse or untreated sample [8, 15–17, 25, 27, 42]. Children younger than 8 years were not enrolled. Age at OCD symptom onset was assessed retrospectively rather than prospectively. Many of the findings are correlational, requiring experimental studies to establish any causal relationships between the variables.

Summary

The ERN and Pe are components of the ERP following an error that are potential mechanistic biomarkers for OCD [5, 7–11, 15, 17–21]. The study examined the ERN, Pe, flanker task accuracy, and clinical measures in 105 OCD cases and 105 matched HC ages 8 to 18 years. Compared to HC, the ERN was increased in OCD cases, TR and NTR OCD cases, and current and past OCD cases. The results support the hypothesis that an enlarged ERN may serve as a transdiagnostic biomarker for OCD, tic disorders, and some anxiety disorders [8, 17–22]. Compared to HC, the ΔPe was *decreased* in OCD cases, TR and NTR OCD cases, and current but not past OCD cases. A lower ΔPe in OCD cases was associated with an earlier age at OCD symptom onset, suggesting an atypical development of the Pc or Pe may be involved in the pathogenesis of pediatric OCD. Compared to HC, flanker task accuracy was *decreased* in OCD cases, TR and NTR OCD cases, and current and past OCD cases, whereas higher flanker task accuracy was associated with increased ERN and ΔPe measures in the total sample. The reduced ΔPe in pediatric OCD may reflect a defect in the post-decisional evidence accumulation process that impairs decision accuracy, decision confidence, and subsequent behavioral adjustments [11, 23, 24]. The reduced ΔPe in current but not past OCD cases and the associations of the ΔPe with obsessive–compulsive symptom severity and OCD symptom onset age suggest that the ΔPe may be more directly involved in the pathogenesis of pediatric OCD than the ERN and that interventions augmenting the ΔPe may diminish OCD symptoms.

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Availability of Data and Materials Data and materials are available upon request to the corresponding author.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical Approval All tasks and procedures were approved by the University of Michigan Medical School Institutional Review Board.

Participants or their parents gave written informed consent in accordance with the Declaration of Helsinki.

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