Biological Psychiatry: CNNI

Archival Report

Impairment of Visual Fixation and Preparatory Saccade Control in Borderline Personality Disorder With and Without Comorbid Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

BACKGROUND: Borderline personality disorder (BPD) is associated with heightened impulsivity, evidenced by increased substance abuse, self-harm, and suicide attempts. Addressing impulsivity in individuals with BPD is a therapeutic objective, but its underlying neural basis in this clinical population remains unclear, partly due to its frequent comorbidity with attention-deficit/hyperactivity disorder (ADHD).

METHODS: We used a response inhibition paradigm—the interleaved pro-/antisaccade task—among adolescents diagnosed with BPD with and without comorbid ADHD (n = 25 and n = 24, respectively) during concomitant video-based eye tracking. We quantified various eye movement response parameters reflective of impulsive action during the task, including delay to fixation acquisition, fixation breaks, anticipatory saccades, and direction errors with express saccade (saccade reaction time: 90–140 ms) and regular saccade latencies (saccade reaction time $>$ 140 ms).

RESULTS: Individuals with BPD exhibited deficient response preparation, as evidenced by reduced visual fixation on task cues and greater variability of saccade responses (i.e., saccade reaction time and peak velocity). The ADHD/BPD group shared these traits and made more anticipatory responses and direction errors with express saccade latencies and reduced error correction.

CONCLUSIONS: Saccadic deficits in BPD and ADHD/BPD stemmed not from an inability to execute antisaccades but rather from inadequate preparation for the upcoming task set. These distinctions may arise due to abnormal signaling in cortical areas like the frontal eye fields, posterior parietal cortex, and anterior cingulate cortex. Understanding these mechanisms could provide insights into targeted interventions focusing on task set preparation to manage response inhibition deficits in BPD and ADHD/BPD.

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Of the 9 traits of borderline personality disorder (BPD) listed in the DSM-5, impulsivity is the most predictive of continued BPD symptoms (1). Impulsivity is associated with an increased likelihood of poor outcomes in individuals with BPD, including self-harm, substance abuse, incarceration, and death by suicide (2–4). Unfortunately, the heterogeneity of behaviors that make up impulsivity has created challenges for the research community to reliably identify neural correlates that underlie this phenomenon in BPD and treat it effectively (5–7). For example, the impulsivity criterion for BPD in the DSM-5 is met by a history of self-damaging behavior in at least 2 of the following domains: spending, sex, substance use, reckless driving, and binge eating (8). In contrast, in attention-deficit/hyperactivity disorder (ADHD), the DSM-5's impulsivity category is described as, "often talks excessively," "often has trouble waiting their turn," and "is often on the go" acting as if "driven by a motor" (8). Impulsivity is described differently still in antisocial personality disorder, gambling disorder, and substance use disorder (8).

To better identify which neural signaling pathways underlie impulsivity in psychiatric disorders like BPD, the use of quantitative tests, with continuous measures and established anatomical correlates in the brain, has been recommended (9,10). The interleaved pro-/antisaccade task (IPAST) is well suited to this role, having characterized changes of executive function across normal development and aging and in neurological and psychiatric populations (11–17). The antisaccade task is a simple but effective measure of inhibitory control because it requires participants to first suppress an automatic eye movement toward a visual target (prosaccade) and then produce a voluntary saccade in the opposite direction of the target (antisaccade). Despite its simplicity, successful completion of the antisaccade requires functioning of multiple brain areas, including the frontal and parietal cortex, visual

cortex, thalamus, basal ganglia, superior colliculus, cerebellum, paramedian pontine reticular formation, and extraocular motor nuclei, making it a useful tool to query brain pathology (18). Deficits in antisaccade performance have been found in clinical pathologies associated with heightened impulsivity, including obsessive-compulsive disorder (19), Tourette syndrome (20), schizophrenia (21), and fetal alcohol spectrum disorders (22,23).

A variety of ocular behaviors in the IPAST reflect impulsivity and result in poor task performance, including 1) looking away from the fixation point (FP) that provides the instruction for an upcoming pro- or antisaccade (fixation breaks), 2) guessing future target locations (anticipatory saccades), and 3) making prosaccades to targets on antisaccade trials (direction errors). Distinct signaling pathways in frontal and basal ganglia regions code these behaviors, and the absence of correlation among these measures suggests that these 3 error types are essentially different (17,24). Thus, careful examination of these behaviors can help quantify impulsivity in BPD and provide insight into the functioning of their associated neural circuitry.

We performed our eye-tracking study with adolescent patients with BPD because this is the developmental stage when BPD symptoms first start to emerge and is therefore an important stage for behavioral characterization. We analyzed patients with BPD and BPD with comorbid ADHD (ADHD/BPD) separately to compare how ocular impulsivity measures differed in these groups. Analysis of BPD based on ADHD comorbidity is especially important given the high rates of co-occurrence (i.e., upward of 50%) (25,26) and previous findings of distinct response inhibition behavior in the 2 groups (27–29). Based on previous evidence of impaired frontolimbic circuits in BPD (30–33), we hypothesized that individuals with BPD and ADHD/BPD would show impaired preparation for the IPAST trial, but not impaired saccade execution. Furthermore, we anticipated reduced antisaccade performance in the BPD group with comorbid ADHD.

METHODS AND MATERIALS

Participants

The research protocol (#PHYS-007-97) received approval from Queen's University Faculty of Health Sciences. The age range for study inclusion was 11 to 18 years. Outpatients who were undergoing dialectical behavior therapy for BPD at Kingston Health Sciences Centre's Division of Child and Youth Mental Health, Canada served as clinical participants. The Structured Clinical Diagnostic Interview for Personality Disorders was used to make BPD diagnoses on the day of study completion. Inclusion criteria are provided in Supplemental Methods. Given that females are more often diagnosed with BPD than males, we recruited age-matched healthy female adolescents for the control group. Control participants had no history of psychiatric or neurological disorders. All participants possessed either normal vision or corrected-to-normal vision. Written consent was obtained from participants ages ≥18 years. For participants <18 years, we obtained oral assent from the participants themselves, and written consent was obtained from their legal guardians. The duration of the experiment was approximately 1 hour. Participants received compensation at a rate of $20/hour for their participation.

Recording and Apparatus

Participants were seated 60 cm away from a 17-inch 1280 × 1024 pixel resolution LCD computer monitor in a dark room to undergo eye tracking. Participants' head position was stabilized using a head rest mounted on the desk, permitting them to rest their chin and forehead comfortably. Details of eye-tracking acquisition can be found in Supplemental Methods.

Interleaved Pro-/Antisaccade Task

The IPAST started with an intertrial interval (ITI) that was 1000 ms in duration and featured a blank background (0.1 cd/m^2). Next, a central FP (0.5° diameter dot, 44 cd/m^2) appeared on screen for 1000 ms. The color of the FP indicated the trial condition (green = prosaccade, red = antisaccade). The FP then disappeared, and the screen was blank for 200 ms (gap period), followed by the appearance of a peripheral target that was 10° to the right or left of central position. On prosaccade trials, participants were instructed to look toward the peripheral target. On antisaccade trials, participants were instructed to look in the equal and opposite direction from the peripheral target (Figure 1). The peripheral target remained on the screen for 1000 ms and was followed by an ITI, indicating a break between trials. Prosaccade and antisaccade trials were pseudorandomly interleaved with equal frequency so that the participant was unaware of the upcoming trial type until the FP was displayed. The IPAST paradigm was about 20 minutes in length and consisted of 2 blocks of 120 trials each with a brief break in between blocks.

Saccade Data Analysis

Pre- and postprocessing of eye-tracking data during the IPAST used custom software developed in the laboratory using

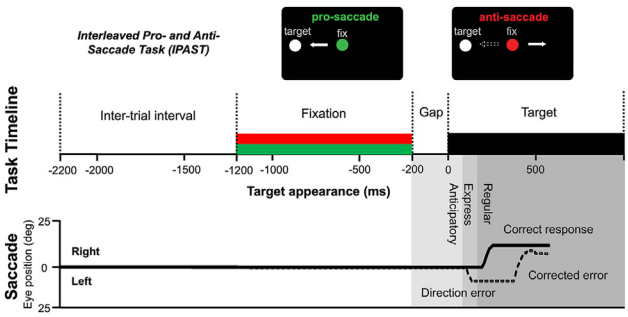

Figure 1. Interleaved pro-/antisaccade task (IPAST) paradigm. Each trial started with a 1000-ms intertrial interval where the screen was blank with a black background. A central fixation point appeared that was either green, indicating a prosaccade trial, or red, indicating an antisaccade trial. The fixation point then disappeared so that the screen was blank for 200 ms. A peripheral target appeared either 10° right or left from the center of the screen. On prosaccade trials, participants were instructed to make a saccade to the peripheral target, and on antisaccade trials, they were instructed to look equal and opposite to the target. The target appeared on screen for 1000 ms prior to the start of a new intertrial interval. A total of 240 trials were recorded, and prosaccade and antisaccade trials were pseudorandomized. Saccades with latencies between −200 and 89 ms relative to target appearance were labeled as anticipatory, 90 to 140 ms as express, and >140 ms as regular. Saccades made toward peripheral targets on antisaccade trials were considered direction errors, and saccades made in the correct direction following an error were considered corrected saccades. deg, degree; fix, fixation.

MATLAB (version R2024a; The MathWorks Inc.). Preprocessing steps of IPAST data have been described in detail elsewhere (34). In the current study, we report on ocular behavior across the entirety of an IPAST trial, including the ITI, FP display, gap period, and peripheral target display. Saccades with reaction times (RTs) <90 ms following target appearance were deemed anticipatory. Saccades with RTs between 90 and 140 ms were defined as express, and those with RTs > 140 ms were labeled as regular. More details on saccade categorization and eye-tracking data analysis, including fixation analysis and calculation of voluntary override time (VOT), can be found in Supplemental Methods.

Statistical Testing and Reporting

Eye-tracking parameters were first averaged for every participant and then again by group (i.e., control, BPD, and ADHD/BPD) to allow for group comparisons. The Shapiro-Wilk test was conducted to assess data normality before performing statistical tests. If the Shapiro-Wilk test yielded nonsignificant results, parametric testing of group comparisons was employed (analysis of variance), and means were reported in the Results section. However, if the Shapiro-Wilk test was significant, nonparametric statistics were utilized (Kruskal-Wallis test), and mean ranks were reported. For significant models, post hoc pairwise comparisons were conducted using Tukey's test for parametric data and the Dunn-Sidak approach for nonparametric data to mitigate type I errors. *p* Values corrected for multiple comparisons were reported. Cohen's *d* effect sizes of significant post hoc results were reported. Spearman rank correlations were used to investigate the relationships among different ocular measures of impulsivity and the Barratt Impulsivity Scale (BIS).

RESULTS

A total of 24 individuals with BPD (mean age = 16.4 years, SD = 1.4), 25 individuals with ADHD/BPD (16.3 ± 1.5 years), and 53 control participants (15.7 ± 1.6 years) were included in the study (Table 1). Age did not differ significantly among groups (p = .109). Comorbid psychiatric diagnoses among clinical participants included major depressive disorder (n = 17), posttraumatic stress disorder (n = 5), anxiety disorders (n = 22), and eating disorders (n = 10). The average BIS scores for the clinical cohorts are displayed in Table 2. The participant group mean percentages of IPAST trials that met the requirements for preprocessing and underwent saccade analysis for the BPD, ADHD/BPD, and control groups were 96.3%, 97.3%, and 98.6%, respectively.

Table 1. Demographic Characteristics of Study Participants

	BPD, n = 24	ADHD/BPD, n = 25	Control, n = 53
Sex, Female, n	24	25	53
Age, Years, Mean ± SD	16.4 ± 1.4	16.3 ± 1.5	15.7 ± 1.6
Impulsivity, Mean ± SD	75.4 ± 8.3	81.8 ± 10.6	65.6 ± 9.7

Impulsivity was measured using the total score of the Barratt Impulsivity Scale.

ADHD, attention-deficit/hyperactivity disorder; BPD, borderline personality disorder.

Table 2. BIS Total and Subscale Scores for the BPD and ADHD/BPD Groups

BIS	BPD, Mean ± SD	ADHD/BPD, Mean ± SD
Total	75.4 ± 8.3	81.8 ± 10.6
Subscale		
Attention	13.0 ± 2.1	14.8 ± 2.9
Cognitive Instability	8.5 ± 2.0	8.7 ± 1.7
Motor	16.5 ± 3.4	19.0 ± 4.0
Perseverance	8.6 ± 2.2	9.1 ± 2.0
Self-control	15.9 ± 4.0	17.1 ± 4.0
Cognitive complexity	13.0 ± 2.0	13.0 ± 2.8

BIS measures did not vary between BPD groups according to presence of an ADHD comorbidity.

ADHD, attention-deficit/hyperactivity disorder; BIS, Barratt Impulsivity Scale; BPD, borderline personality disorder.

Preparation for Task Set

Group fixation acquisition is shown as the average of participants' cumulative density function curves in Figure 2. Regardless of group, approximately 25% of study participants were already fixating on the center of the screen at the start of the ITI. However, both the BPD and ADHD/BPD groups were slower to increase their central fixation in preparation for the next trial start. Fixation acquisition at FP appearance (−1200 ms relative to target appearance) differed significantly by group (χ^2_2 = 13.81, p = .001) (Figure 2B) such that control participants were more likely to be at central fixation by the time of its

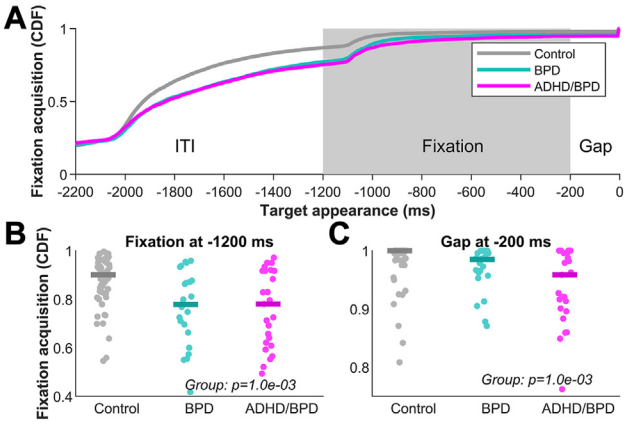

Figure 2. Cumulative acquisition of visual fixation to central position prior to peripheral target appearance in the interleaved pro-/antisaccade task. **(A)** Mean cumulative density function (CDF) of fixation to screen center of borderline personality disorder (BPD) (in blue), attention-deficit/hyperactivity disorder (ADHD)/BPD (in pink), and control (in gray) participant groups across the 1000-ms duration of the intertrial interval (ITI) (−2200 to −1200 ms, relative to target appearance), fixation point display (−1200 to −200 ms), and gap period (−200 to 0 ms). **(B)** Individual participants' mean CDF at the start of the fixation point display period is shown as circle markers, and the group median is displayed as a horizontal bar. A main effect of participant group on mean CDF was found (χ^2_2 = 13.81, p = .001), with significant post hoc comparisons revealing reduced fixation acquisition of the BPD and ADHD/BPD groups compared with the control group. **(C)** A main effect of fixation acquisition was found at the start of the gap period (χ^2_2 = 13.81, p = .001), with reduced fixation acquisition observed in both BPD and ADHD/BPD groups.

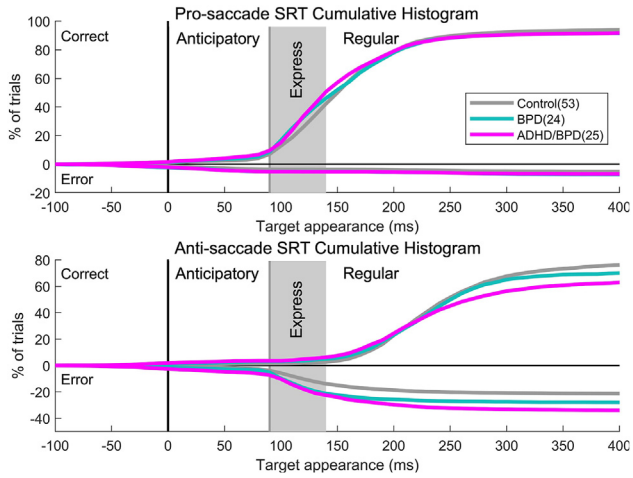

Figure 3. Cumulative distribution of saccade reaction times on pro- and antisaccade trials. The vertical black line at 0 ms represents time of target appearance, with saccade latencies occurring from 0 to 89 ms being classified as anticipatory, 90 to 140 ms as express (gray bar epoch), and >140 ms as regular. Positive cumulative traces reflect saccades that were correctly made toward the target (i.e., prosaccade trial) or away from the target (i.e., antisaccade trial). Negative cumulative traces reflect erroneous saccade trials. Participants with attention-deficit/hyperactivity disorder (ADHD)/borderline personality disorder (BPD) made more direction errors, with the majority of errors occurring in the anticipatory saccade window.

appearance than participants in the BPD group (p = .0173, Cohen's d = 0.764) and the ADHD/BPD group (p = .004, Cohen's d = 0.863). This main effect was found again at gap onset (χ^2_2 = 13.81, p = .001) (Figure 2C). Control participants were more likely to be at central fixation at the start of the gap period than individuals with BPD (p = .035, Cohen's d = 0.475) and ADHD/BPD (p = .002, Cohen's d = 0.616). The BPD and ADHD/BPD groups did not differ from one another in their fixation acquisition behavior.

Cumulative reaction time distributions of saccadic responses on pro- and antisaccade trials are shown in Figure 3. There was a main effect of group on fixation breaks (i.e., saccades away from fixation that did not return before the end of the fixation epoch) (χ^2_2 = 22.65, p = 1.21 × 10^{-5}) (Figure 4A). Compared with control participants (mean rank = 84.3), participants in both BPD (mean rank = 114.8, p = .009, Cohen's d = 0.445) and ADHD/BPD groups (mean rank = 129.3, p = 2.44 × 10^{-5}, Cohen's d = 0.666) made more fixation breaks. There was no significant difference between the BPD and ADHD/BPD groups (p = .529). Fixation break frequency did not vary by FP instruction (i.e., prosaccade vs. antisaccade). The percentage of IPAST trials with anticipatory saccades differed significantly by group (χ^2_2 = 11.65, p = .003) (Figure 4B). Individuals with ADHD/BPD (mean rank = 124.04) made significantly more anticipatory saccades than control participants (mean rank = 90.16, p = .002, Cohen's d = 0.537); no other pairwise comparisons were significant. All groups showed increased anticipatory saccades for an upcoming prosaccade trial than for an antisaccade trial (χ^2_1 = 16.18, p = 5.78 × 10^{-5}) (Figure 4B). There was a main effect of group × ratio of total erroneous antisaccades (χ^2_2 = 8.19, p = .0167), with post hoc tests revealing significant differences between the ADHD/BPD (mean rank = 64.78) and control groups (mean rank = 44.40) (p = .0135, Cohen's d = 0.775). These data correspond to a mean antisaccade error rate of 19.64% ± 11.69% in the control group, 26.68% ± 19.82% in the BPD group, and 32.70% ± 20.76 in ADHD/BPD group. Express saccade direction errors differed significantly by group (χ^2_2 = 8.24, p = .0163) (Figure 4C), with significantly more express saccade direction errors in the ADHD/BPD group than the control group (mean rank = 43.44, p = .039, Cohen's d = 0.606). The pairwise comparison between the BPD and control groups was nonsignificant.

Execution of Task Set

The ratio of regular saccade direction errors did not differ by group (p = .164). There was no main effect of group on the median saccade RT (SRT) for pro- or antisaccades (Figure 5A). The SRT coefficient of variation (CV) did vary significantly by group (χ^2_2 = 22.78, p = 1.13 × 10^{-5}) (Figure 5B), with larger CV values for the BPD and ADHD/BPD groups than the control

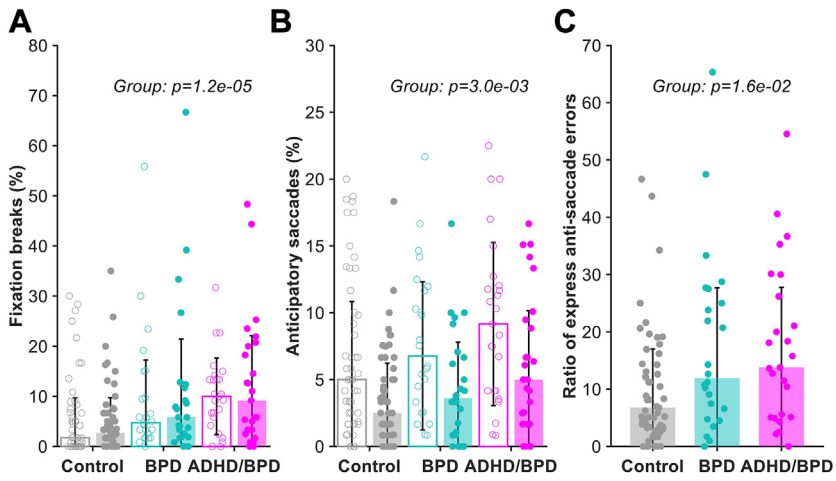

Figure 4. Fixation breaks, anticipatory saccades, and express direction errors by participant group. **(A)** Circle markers display the mean percentage of trials with fixation breaks per individual participant, and the horizontal bars show the group median. Unfilled circles and bars reflect prosaccade trials, and filled circles and bars reflect antisaccade trials. A main effect of participant group on the percentage of trials with fixation breaks was observed (χ^2_2 = 22.65, p = 1.21 × 10^{-5}). Fixation breaks did not vary by task condition (i.e., prosaccade vs. antisaccade). **(B)** The percentage of trials with anticipatory saccades differed significantly by group, (χ^2_2 = 11.65, p = .003) and task condition (i.e., prosaccade vs. antisaccade) (χ^2_1 = 16.18, p = 5.78 × 10^{-5}). **(C)** Ratio of direction errors with express saccade latencies (saccade reaction time: 90 to 140 ms, inclusive) on antisaccade trials varying significantly by participant group (χ^2_2 = 8.24, p = .0163). ADHD, attention-deficit/hyperactivity disorder; BPD, borderline personality disorder.

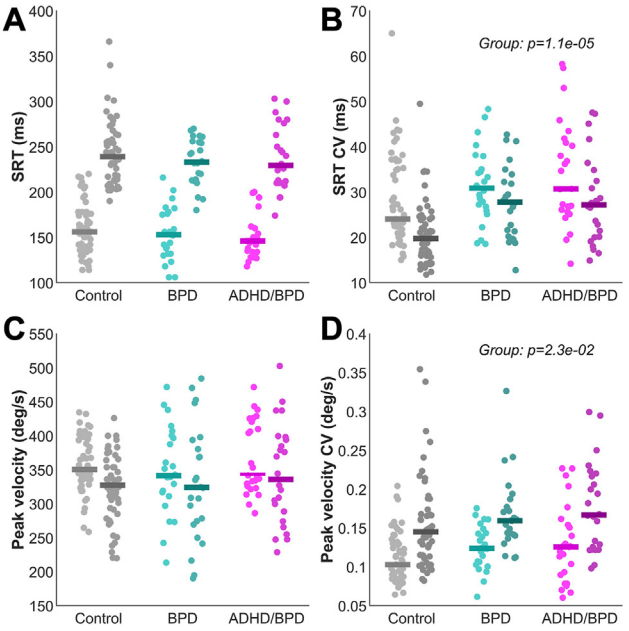

Figure 5. Saccade metrics in the interleaved pro-/antisaccade task by participant group. **(A)** Mean participants' saccade reaction times (SRTs) to peripheral targets are displayed as circles, and horizontal bars reflect the group median. Light colored circles and bars reflect correct prosaccade trials, and dark colored circles and bars reflect correct antisaccade trials. As expected, SRTs were significantly longer for antisaccade trials than for prosaccade trials. There was no effect of participant group on SRT. **(B)** Variability of SRTs, measured by the coefficient of variation (CV), varied significantly by group ($\chi^2_2 = 22.78$, $p = 1.13 \times 10^{-5}$), with larger SRT CV measures in the borderline personality disorder (BPD) and attention-deficit/hyperactivity disorder (ADHD)/BPD groups than the control group. **(C)** Peak velocity did not differ by group membership; however, the **(D)** CV of peak velocity did differ significantly by group ($\chi^2_2 = 7.56$, $p = .023$).

group ($p = 5.33 \times 10^{-4}$, Cohen's $d = 0.585$ and $p = 2.06 \times 10^{-4}$, Cohen's $d = 0.655$, respectively). Similarly, peak saccadic velocity did not differ by group (Figure 5C), whereas the CV of peak saccadic velocity did ($\chi^2_2 = 7.56$, $p = .023$) (Figure 5D); however, the post hoc analysis was nonsignificant. No main effects of group were observed on saccade amplitude ($p = .070$) or amplitude CV ($p = .076$).

The number of direction errors and number of corrected direction errors (i.e., saccades to the correct location following an error) were plotted for each participant (Figure 6A). Figure 6B shows that the averaged polynomial fits varied by group ($\chi^2_2 = 11.82$, $p = .0027$), with differences between the ADHD/BPD and control groups ($p = .042$), indicating that participants with ADHD/BPD corrected fewer errors. Furthermore, the intersaccade interval (ISI) between the end of a direction error and the onset of a corrective saccade varied by group ($p = .02$) (Figure 7), with a significantly longer average ISI in the ADHD/BPD group than in the control group. Voluntary override time (VOT) did not interact with group (see Figure 8 for the VOT cumulative distribution curves and mean VOT).

Correlations Among Impulsivity Measures

Self-report measures of impulsivity in BPD groups assessed by the BIS total score and subscale scores were not

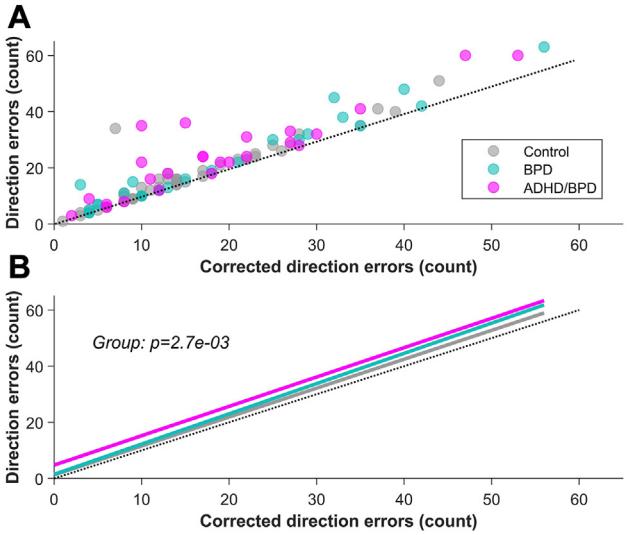

Figure 6. Polynomial fits of corrected direction errors vs. total direction errors. **(A)** Participants' number of direction errors on antisaccade trials (y-axis) plotted against participant's number of corrected saccades (x-axis). **(B)** Polynomial fits were applied to panel **(A)** data, and the average fit for each participant group is plotted. The dotted black line is a meridian line with a slope of 1, meaning that there is a corresponding corrected saccade for every direction error. Polynomial fits differed significantly for the attention-deficit/hyperactivity disorder (ADHD)/borderline personality disorder (BPD) group vs. the BPD and control groups, supporting fewer corrective saccades following direction errors.

significantly correlated with ocular performance measures of fixation breaks, anticipatory saccades, or express or regular latency direction errors.

DISCUSSION

We interpreted differences in saccade performance across the IPAST paradigm as 1) failure to prepare for a task set (i.e., fixation acquisition, fixation breaks, anticipatory saccades, and express direction errors) versus 2) failure to execute a task set (i.e., saccade metrics [e.g., SRT, peak velocity, amplitude], regular direction errors, VOT, and corrective saccades) and discuss associated oculomotor circuits and theorize as to how they could be impacted in adolescent BPD with and without comorbid ADHD. We found substantial differences between both the BPD and ADHD/BPD groups and the control group in the preparation for eye movements. However, the actual execution of eye movements was similar among groups. The ADHD/BPD group displayed reduced response inhibition performance compared to the control group, above and beyond that of the BPD group, as evidenced by increased direction errors and fewer and delayed correction of errors.

Preparation for the Task Set

Impaired Fixation in BPD and ADHD/BPD. BPD and ADHD/BPD groups showed delayed fixation acquisition compared to age- and sex-matched control group, corresponding with large effect sizes (Cohen's $d = 0.764$ and 0.863, respectively) (Figure 2B). Both BPD groups showed increased fixation breaks. To our knowledge, this study is the first to

Biological Psychiatry: CNNI

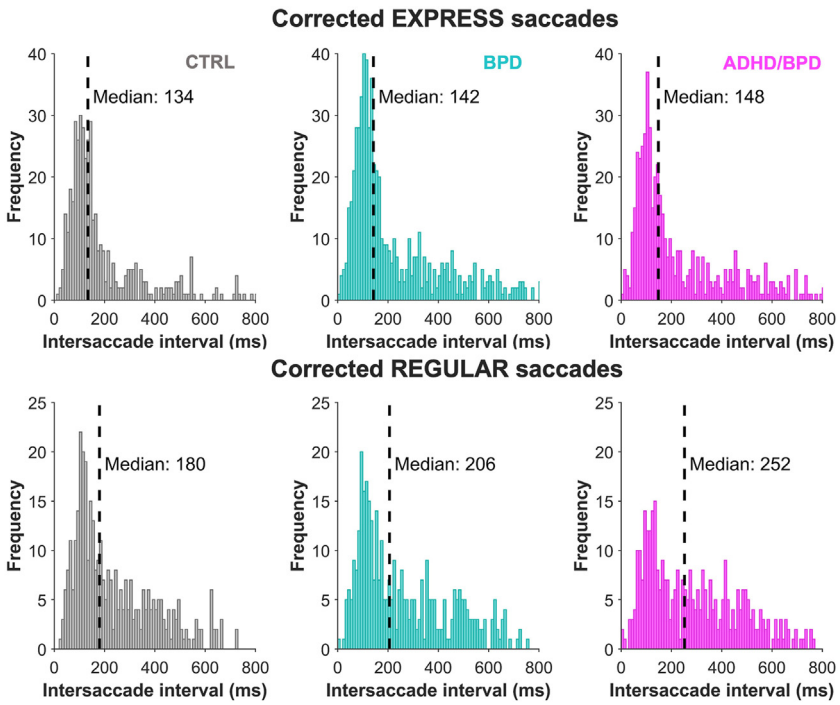

Figure 7. Timing of saccade correction on erroneous antisaccade trials. Distribution of intersaccade intervals between direction errors and corrected saccades following erroneous express saccades (top row) and erroneous regular saccades (bottom row). There was a main effect of participant group × intersaccadic interval (χ^2_2 = 7.17, p = .0277), with participants with attention-deficit/hyperactivity disorder (ADHD)/borderline personality disorder (BPD) taking significantly longer to make a corrective saccade than participants with BPD alone and control (CTRL) participants (p = .0216).

describe abnormal fixation behavior in BPD; however, previous work has noted increased frequency of intrusive saccades in ADHD during periods of fixation in a prosaccade task (35), a go/no-go task (36), and a peripheral target distractor task (37,38). In the antisaccade task, Loe *et al.* varied the duration of the FP (0.5–6 seconds) (37). They found that longer fixation durations led to higher SRTs and fewer direction errors. However, this effect was absent in the ADHD group. Based on our data, we suggest that inadequate fixation or failure to achieve optimal fixation before the gap onset hinders the inhibitory effect of saccades on saccade initiation in ADHD (39).

There was no task effect on fixation acquisition or fixation breaks (Figure 2), indicating that fixation impairments are not caused by aberrant top-down signaling necessary for antisaccade production. The posterior parietal cortex (PPC) likely underlies the behavior of poor fixation in BPD and ADHD/BPD given its fixation-related excitability (40–42) and discharge properties similar to those of fixation cells in the intermediate

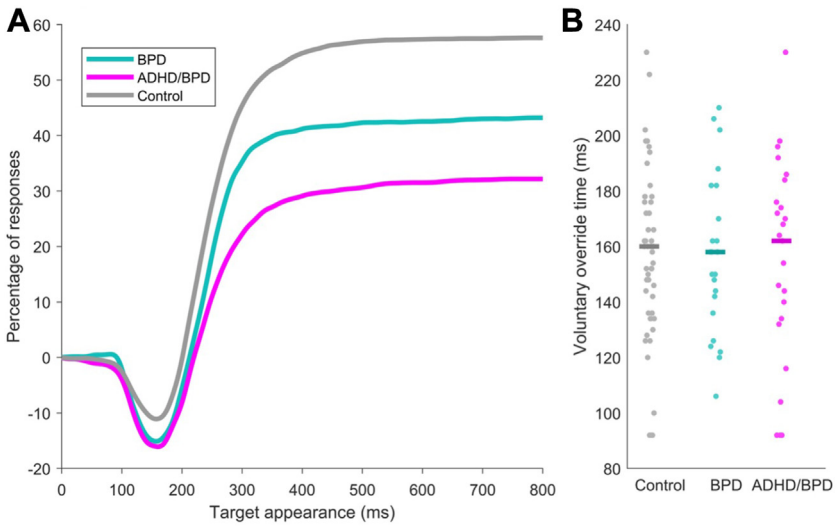

Figure 8. Voluntary override time by participant group. **(A)** Mean cumulative saccade reaction time distributions for direction error antisaccade trials subtracted by correct antisaccade trials per participant group. The minimum point of the cumulative distribution was calculated per individual participant, averaged across trials, and displayed as circular markers in **(B)** as voluntary override time. This measure is an estimate of the amount of time that it takes for the voluntary signal to outcompete the automatic signal to generate an antisaccade in the direction opposite of the peripheral target. There was no main effect of group type on voluntary override time. ADHD, attention-deficit/hyperactivity disorder; BPD, borderline personality disorder.

layer of superior colliculus (SCi) (43). Diminished activity of visual PPC neurons may explain our findings of fixation instability in both groups because the parietal lobe is highly implicated in BPD [see Swinton (44) for a review], with multiple studies reporting structurally smaller parietal cortices in BPD (45–48) and abnormal metabolic signaling (49). Furthermore, hypoactivity of the parietal lobe has been documented in ADHD during response inhibition tasks (50–52). The frontal eye fields (FEFs) also demonstrate neuronal activity specific to visual fixation, and stimulation of their fixation cell sites results in bilateral saccade suppression (53,54). Fixation breaks have been likened to task disengagement or reduced motivation because they were found to be correlated with attention/working memory scores and executive function scores (17). Worsened fixation may reflect an overall reduced attentional state in BPD and ADHD/BPD that corresponds with diminished fixation-related activity within cortical areas of the PPC and FEFs that relay input to the SCi to maintain fixation in preparation for the start of the task.

Increased Anticipatory Responses in ADHD/BPD. Consistent with the results of our previous study (27), we observed that when ADHD comorbidity was controlled for, there was no difference between the BPD and control groups in their percentage of anticipatory saccades. Our finding of increased premature responses in the comorbid ADHD group is consistent with previous research that has supported an impaired ability to wait for trial start prior to motor action (36,55,56). However, our results in the BPD group differ from those of a previous antisaccade study that cited more anticipatory saccades in individuals with BPD than in control individuals (57). We attribute this difference to the range of SRTs that were considered anticipatory, with ours being 0 to 89 ms relative to target appearance and that of Grooten *et al.* (57) being −500 to 80 ms, which likely included fixation breaks. Furthermore, a comorbid ADHD diagnosis was not excluded, so it is unknown whether or to what extent comorbid ADHD pathology influenced the results. Our findings also differ from those of Parr *et al.* (58), who found increased anticipatory action in BPD; however, we credit this discrepancy to several key differences in task design and task demands, which are discussed in the Supplemental Discussion.

Increased anticipatory motor action during IPAST has been observed in macaques following injection of muscimol to the rostral SCi, resulting in reduced fixation cell excitability (39). Similar to our results (Figure 4B), that study reported an anti-effect on fixation cell firing that corresponded with fewer anticipatory saccades on antisaccade trials (39). Therefore, increased anticipatory saccades in ADHD/BPD likely reflects reduced cortical inhibition to SCi before trial start, which results in excessive premotor activity that overlaps with the cortico-striato-thalamocortical loop of the oculomotor circuit (59), specifically aberrant signaling of the PPC and prefrontal cortex.

Increased Express Direction Errors in ADHD/BPD. Compared with control participants, express direction errors were increased in participants with ADHD/BPD (Figure 4C); however, this was not observed in BPD alone. Of the 2 antisaccade studies performed previously in BPD, one noted no difference compared with control participants, consistent with our results, and the other reported increased errors (57). The Grootens *et al.* study (57) did not exclude participants with an ADHD comorbidity, and the type of direction errors were pooled (i.e., express and regular); therefore, a direct study comparison is limited. To prevent an express direction error, visuomotor cell activity in the SCi must have reduced excitability prior to target appearance (60,61). If this activity is not adequately reduced during this preparatory period, the visual transient signal will be strong enough to evoke a fast prosaccade to the peripheral target, resulting in a direction error. Brain areas that are important for relaying preemptive inhibitory firing to prevent the peripheral visual stimulus from triggering a saccadic command are the FEFs and fixation cells in the SCi. Individuals with lesions in the dorsolateral prefrontal cortex, including FEF areas, generate increased direction errors, mainly with express saccade latencies (16). Other neural regions that show enhanced pre-target activity during antisaccade trials versus prosaccade trials include the caudate nucleus and the external segment of the globus pallidus (62,63).

Based on our results, we theorize that dysfunctional preparatory signaling of frontal structures, such as the FEFs, and possibly striatal areas, underlie the behavioral result of increased express saccade errors in the ADHD/BPD group. This result is again consistent with impairment of signaling within the oculomotor circuit (59). Age-based modeling supports that express errors increase from childhood, peaking at 9 to 11 years and then decreasing until the early twenties and remaining steady into old age (24), reflecting the maturation of automated pathways to make an express saccade by mid-childhood and delayed maturation of top-down preparatory suppression signals until early adulthood. Because we collected our data from adolescents, it is unknown whether the maturation of this circuitry is delayed in the comorbid ADHD cohort and becomes normal in adulthood or whether it remains irregular into adulthood, thus warranting future research. In an IPAST study of multiple neurodegenerative diseases, the finding of increased express errors was not observed in any of them (17); however, 5 of the 12 disease subgroups showed increased regular direction errors. Thus, the impairment of preparatory inhibitory signaling necessary to prevent an express direction error may be more specific to the circuitry of psychopathology versus that of neurodegenerative disease.

Execution of the Task Set

Normal Regular Direction Errors and VOT in Individuals With BPD With and Without ADHD. Regular latency direction errors did not differ between people with BPD and ADHD/BPD compared with control participants, supporting an intact ability of the voluntary motor signal to override the automatic signal to successfully make an antisaccade. Brain areas that relay the voluntary saccade command to inhibit the automatic command located on the side contralateral to the visual stimulus include the supplementary eye field and basal ganglia (64,65). Our result that the VOT was normal in BPD and ADHD/BPD further supports this result. These findings reaffirm that deficits in antisaccade performance in ADHD are related to reduced preparatory control from frontal structures to the SCi

to inhibit saccade neurons. If properly inhibited, however, the voluntary saccade command is successfully generated via frontostriatal circuits. This result is consistent with multiple studies that have reported no difference in performance execution or corresponding metabolic blood oxygen level–dependent activity in BPD alone during response inhibition tasks (28,29,66–71). Consistent with the literature, we found no group effect on median saccade latencies, peak velocity, or amplitude (27,37,50,56,57), supporting that differences in group performance are driven by differences in higher-level cognition rather than sensorimotor function. Like other studies in BPD (29,58), ADHD/BPD (29,58), and ADHD (35,50,55,56), SRT and peak velocity variability were increased in BPD and ADHD/BPD, supporting diminished task preparation.

Reduced Error Correction and Delayed Timing of Correction in ADHD/BPD. Participants in the ADHD/BPD group corrected fewer errors than the other groups. This could be the result of a failure to identify that an error had been made or a lack of motivation to correct the error. In an IPAST functional magnetic resonance imaging study, individuals with ADHD corrected 75.8% of their antisaccade errors versus 90.6% in control participants (50). Of the corrected saccades, the ADHD group showed reduced metabolic activity of the anterior cingulate cortex compared with control participants, which is involved in the processing and monitoring of errors. It is possible that hypoactivation of the anterior cingulate cortex in the ADHD/BPD group underlies our result of fewer error corrections. These results are further supported by our finding of an increased gap between the timing of an error and its correction in the ADHD/BPD group (Figure 7). Whether this reflects a longer processing time to recognize an error or an increased time to initiate its correction requires further testing.

Correlations Among Ocular and Clinical Impulsivity Measures

Our quantitative measures of impulsive action did not correlate with BIS self-report scales of impulsivity, consistent with previous work (27,67,72,73). Similarly, despite there being differences in task response metrics between the BPD and ADHD/BPD groups, impulsivity as assessed by the BIS did not vary. These findings support the use of continuous measures of impulsivity using performance tasks over self-report questionnaires to establish the nuances of impulsive action and their neural correlates.

Conclusions

IPAST performance in adolescent BPD and ADHD/BPD indicated reduced fixation behavior and impaired preparatory signaling prior to task instruction, which resulted in increased premature responses and short-latency errors in ADHD/BPD and diminished error correction in ADHD/BPD. Together, these results implicate aberrant signaling of the PPC and FEFs in individuals with BPD with and without comorbid ADHD during visual fixation. Participants with BPD and comorbid ADHD showed additional impairments of oculomotor circuitry function, likely involving frontal cortical regions of the dorsolateral prefrontal cortex and FEFs. Study limitations can be found in the Supplemental Discussion.

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REFERENCES

1. Links PS, Heslegrave R, van Reekum R (1999): Impulsivity: Core aspect of borderline personality disorder. J Pers Disord 13:1–9.
2. Sebastian A, Retz W, Tüscher O, Turner D (2019): Violent offending in borderline personality disorder and attention deficit/hyperactivity disorder. Neuropharmacology 156:107565.
3. Bornovalova MA, Lejuez CW, Daughters SB, Zachary Rosenthal MZ, Lynch TR (2005): Impulsivity as a common process across borderline personality and substance use disorders. Clin Psychol Rev 25:790–812.
4. Gunderson JG, Herpertz SC, Skodol AE, Torgersen S, Zanarini MC (2018): Borderline personality disorder. Nat Rev Dis Primers 4:18029.
5. Sebastian A, Jung P, Krause-Utz A, Lieb K, Schmahl C, Tüscher O (2014): Frontal dysfunctions of impulse control – A systematic review in borderline personality disorder and attention-deficit/hyperactivity disorder. Front Hum Neurosci 8:698.
6. Gagnon J (2017): Defining borderline personality disorder impulsivity: Review of neuropsychological data and challenges that face researchers. J Psychiatry Psychiatric Disord 01:154–176.
7. Barker V, Romaniuk L, Cardinal RN, Pope M, Nicol K, Hall J (2015): Impulsivity in borderline personality disorder. Psychol Med 45:1955–1964.
8. American Psychological Association (2013): Diagnostic and Statistical Manual of Mental Disorders, 5th ed: DSM-5. Washington, DC: American Psychiatric Association.
9. Cuthbert BN, Insel TR (2013): Toward the future of psychiatric diagnosis: The seven pillars of RDoC. BMC Med 11:126.
10. Kotov R, Krueger RF, Watson D, Cicero DC, Conway CC, DeYoung CG, *et al.* (2021): The hierarchical taxonomy of psychopathology (HiTOP): A quantitative nosology based on consensus of evidence. Annu Rev Clin Psychol 17:83–108.
11. Munoz DP, Broughton JR, Goldring JE, Armstrong IT (1998): Age-related performance of human subjects on saccadic eye movement tasks. Exp Brain Res 121:391–400.

12. Chan F, Armstrong IT, Pari G, Riopelle RJ, Munoz DP (2005): Deficits in saccadic eye-movement control in Parkinson's disease. Neuropsychologia 43:784–796.
13. Huang LY, Jackson BS, Rodrigue AL, Tamminga CA, Gershon ES, Pearlson GD, *et al.* (2022): Antisaccade error rates and gap effects in psychosis syndromes from bipolar-schizophrenia network for intermediate phenotypes 2 (B-SNIP2). Psychol Med 52:2692–2701.
14. Yep R, Smorenburg ML, Riek HC, Calancie OG, Kirkpatrick RH, Perkins JE, *et al.* (2022): Interleaved pro/anti-saccade behavior across the lifespan. Front Aging Neurosci 14:842549.
15. Yep R, Soncin S, Brien DC, Coe BC, Marin A, Munoz DP (2018): Using an emotional saccade task to characterize executive functioning and emotion processing in attention-deficit hyperactivity disorder and bipolar disorder. Brain Cogn 124:1–13.
16. Guitton D, Buchtel HA, Douglas RM (1985): Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. Exp Brain Res 58:455–472.
17. Riek HC, Brien DC, Coe BC, Huang J, Perkins JE, Yep R, *et al.* (2023): Cognitive correlates of antisaccade behaviour across multiple neurodegenerative diseases. Brain Commun 5:fcad049.
18. Munoz DP, Everling S (2004): Look away: The anti-saccade task and the voluntary control of eye movement. Nat Rev Neurosci 5:218–228.
19. Lennertz L, Rampacher F, Vogeley A, Schulze-Rauschenbach S, Pukrop R, Ruhrmann S, *et al.* (2012): Antisaccade performance in patients with obsessive–compulsive disorder and unaffected relatives: Further evidence for impaired response inhibition as a candidate endophenotype. Eur Arch Psychiatry Clin Neurosci 262:625–634.
20. Jahanshahi M, Rothwell JC (2017): Inhibitory dysfunction contributes to some of the motor and non-motor symptoms of movement disorders and psychiatric disorders. Philos Trans R Soc B Biol Sci 372: 20160198.
21. Cutsuridis V, Smyrnis N, Evdokimidis I, Perantonis S (2007): A neural model of decision-making by the superior colicullus in an antisaccade task. Neural Netw 20:690–704.
22. Green CR, Munoz DP, Nikkel SM, Reynolds JN (2007): Deficits in eye movement control in children with fetal alcohol spectrum disorders. Alcohol Clin Exp Res 31:500–511.
23. Paolozza A, Titman R, Brien D, Munoz DP, Reynolds JN (2013): Altered accuracy of saccadic eye movements in children with fetal alcohol spectrum disorder. Alcohol Clin Exp Res 37:1491–1498.
24. Coe BC, Munoz DP (2017): Mechanisms of saccade suppression revealed in the anti-saccade task. Philos Trans R Soc B Biol Sci 372: 20160192.
25. Fossati A, Novella L, Donati D, Donini M, Maffei C (2002): History of childhood attention deficit/hyperactivity disorder symptoms and borderline personality disorder: A controlled study. Compr Psychiatry 43:369–377.
26. Philipsen A, Limberger MF, Lieb K, Feige B, Kleindienst N, Ebner-Priemer U, *et al.* (2008): Attention-deficit hyperactivity disorder as a potentially aggravating factor in borderline personality disorder. Br J Psychiatry 192:118–123.
27. Calancie OG, Parr AC, Brien DC, Huang J, Pitigoi IC, Coe BC, *et al.* (2023): Motor synchronization and impulsivity in pediatric borderline personality disorder with and without attention-deficit hyperactivity disorder: An eye-tracking study of saccade, blink and pupil behavior. Front Neurosci 17:1179765.
28. Nigg JT, Silk KR, Stavro G, Miller T (2005): Disinhibition and borderline personality disorder. Dev Psychopathol 17:1129–1149.
29. Lampe K, Konrad K, Kroener S, Fast K, Kunert HJ, Herpertz SC (2007): Neuropsychological and behavioural disinhibition in adult ADHD compared to borderline personality disorder. Psychol Med 37:1717–1729.
30. Safar K, Sato J, Ruocco AC, Korenblum MS, O'Halpin H, Dunkley BT (2019): Disrupted emotional neural circuitry in adolescents with borderline personality traits. Neurosci Lett 701:112–118.
31. Vandekerckhove M, Berens A, Wang YL, Quirin M, De Mey J (2020): Alterations in the fronto-limbic network and corpus callosum in borderline-personality disorder. Brain Cogn 138:103596.
32. Soloff PH, Pruitt P, Sharma M, Radwan J, White R, Diwadkar VA (2012): Structural brain abnormalities and suicidal behavior in borderline personality disorder. J Psychiatr Res 46:516–525.
33. Minzenberg MJ, Fan J, New AS, Tang CY, Siever LJ (2007): Fronto-limbic dysfunction in response to facial emotion in borderline personality disorder: An event-related fMRI study. Psychiatry Res 155:231–243.
34. Coe BC, Huang J, Brien DC, White BJ, Yep R, Munoz DP (2024): Automated analysis pipeline for extracting saccade, pupil, and blink parameters using video-based eye tracking. Vision (Basel) 8:1–20.
35. Munoz DP, Armstrong IT, Hampton KA, Moore KD (2003): Altered control of visual fixation and saccadic eye movements in attention-deficit hyperactivity disorder. J Neurophysiol 90:503–514.
36. Castellanos FX, Marvasti FF, Ducharme JL, Walter JM, Israel ME, Krain A, *et al.* (2000): Executive function oculomotor tasks in girls with ADHD. J Am Acad Child Adolesc Psychiatry 39:644–650.
37. Loe IM, Feldman HM, Yasui E, Luna B (2009): Oculomotor performance identifies underlying cognitive deficits in attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 48: 431–440.
38. Caldani S, Razuk M, Septier M, Barela JA, Delorme R, Acquaviva E, Bucci MP (2018): The effect of dual task on attentional performance in children with ADHD. Front Integr Neurosci 12:67.
39. Munoz DP, Wurtz RH (1993): Fixation cells in monkey superior colliculus. II. Reversible activation and deactivation. J Neurophysiol 70:576–589.
40. Paré M, Wurtz RH (1997): Monkey posterior parietal cortex neurons antidromically activated from superior colliculus. J Neurophysiol 78:3493–3497.
41. Mountcastle VB, Andersen RA, Motter BC (1981): The influence of attentive fixation upon the excitability of the light-sensitive neurons of the posterior parietal cortex. J Neurosci 1:1218–1225.
42. Lynch JC, Mountcastle VB, Talbot WH, Yin TCT (1977): Parietal lobe mechanisms for directed visual attention. J Neurophysiol 40: 362–389.
43. Munoz DP, Wurtz RH (1993): Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. J Neurophysiol 70:559–575.
44. Swinton M (2003): The role of the parietal lobe in borderline personality disorder. Med Hypotheses 60:263–267.
45. Hazlett EA, New AS, Newmark R, Haznedar MM, Lo JN, Speiser LJ, *et al.* (2005): Reduced anterior and posterior cingulate gray matter in borderline personality disorder. Biol Psychiatry 58:614–623.
46. Irle E, Lange C, Sachsse U (2005): Reduced size and abnormal asymmetry of parietal cortex in women with borderline personality disorder. Biol Psychiatry 57:173–182.
47. Irle E, Lange C, Weniger G, Sachsse U (2007): Size abnormalities of the superior parietal cortices are related to dissociation in borderline personality disorder. Psychiatry Res 156:139–149.
48. Richter J, Brunner R, Parzer P, Resch F, Stieltjes B, Henze R (2014): Reduced cortical and subcortical volumes in female adolescents with borderline personality disorder. Psychiatry Res 221:179–186.
49. Lange C, Kracht L, Herholz K, Sachsse U, Irle E (2005): Reduced glucose metabolism in temporo-parietal cortices of women with borderline personality disorder. Psychiatry Res 139:115–126.
50. Hakvoort Schwerdtfeger RM, Alahyane N, Brien DC, Coe BC, Stroman PW, Munoz DP (2012): Preparatory neural networks are impaired in adults with attention-deficit/hyperactivity disorder during the antisaccade task. NeuroImage Clin 2:63–78.
51. Schneider MF, Krick CM, Retz W, Hengesch G, Retz-Junginger P, Reith W, Rösler M (2010): Impairment of fronto-striatal and parietal cerebral networks correlates with attention deficit hyperactivity disorder (ADHD) psychopathology in adults – A functional magnetic resonance imaging (fMRI) study. Psychiatry Res 183:75–84.
52. Smith AB, Taylor E, Brammer M, Toone B, Rubia K (2006): Task-specific hypoactivation in prefrontal and temporoparietal brain regions during motor inhibition and task switching in medication-naive children and adolescents with attention deficit hyperactivity disorder. Am J Psychiatry 163:1044–1051.

53. Bizzi E (1968): Discharge of frontal eye field neurons during saccadic and following eye movements in unanesthetized monkeys. Exp Brain Res 6:69–80.
54. Izawa Y, Suzuki H, Shinoda Y (2004): Suppression of visually and memory-guided saccades induced by electrical stimulation of the monkey frontal eye field. I. Suppression of ipsilateral saccades. J Neurophysiol 92:2248–2260.
55. Feifel D, Farber RH, Clementz BA, Perry W, Anllo-Vento L (2004): Inhibitory deficits in ocular motor behavior in adults with attention-deficit/hyperactivity disorder. Biol Psychiatry 56:333–339.
56. Carr LA, Nigg JT, Henderson JM (2006): Attentional versus motor inhibition in adults with attention-deficit/hyperactivity disorder. Neuropsychology 20:430–441.
57. Grootens KP, van Luijtelaar G, Buitelaar JK, van der Laan A, Hummelen JW, Verkes RJ (2008): Inhibition errors in borderline personality disorder with psychotic-like symptoms. Prog Neuropsychopharmacol Biol Psychiatry 32:267–273.
58. Parr AC, Calancie OG, Coe BC, Khalid-Khan S, Munoz DP (2021): Impulsivity and emotional dysregulation predict choice behavior during a mixed-strategy game in adolescents with borderline personality disorder. Front Neurosci 15:667399.
59. Alexander GE, Crutcher MD, Delong MR (1990): Basal ganglia-thalamocortical circuits: Parallel substrates for motor, oculomotor, "prefrontal"; and "limbic"; functions. Prog Brain Res 85:119–149.
60. Everling S, Dorris MC, Munoz DP (1998): Reflex suppression in the anti-saccade task is dependent on prestimulus neural processes. J Neurophysiol 80:1584–1589.
61. Everling S, Dorris MC, Klein RM, Munoz DP (1999): Role of primate superior colliculus in preparation and execution of anti-saccades and pro-saccades. J Neurosci 19:2740–2754.
62. Watanabe M, Munoz DP (2009): Neural correlates of conflict resolution between automatic and volitional actions by basal ganglia. Eur J Neurosci 30:2165–2176.
63. Watanabe M, Munoz DP (2010): Presetting basal ganglia for volitional actions. J Neurosci 30:10144–10157.
64. Parton A, Nachev P, Hodgson TL, Mort D, Thomas D, Ordidge R, *et al.* (2007): Role of the human supplementary eye field in the control of saccadic eye movements. Neuropsychologia 45:997–1008.
65. Chapman BB, Corneil BD (2014): Short-duration stimulation of the supplementary eye fields perturbs anti-saccade performance while potentiating contralateral head orienting. Eur J Neurosci 39: 295–307.
66. Jacob GA, Zvonik K, Kamphausen S, Sebastian A, Maier S, Philipsen A, *et al.* (2013): Emotional modulation of motor response inhibition in women with borderline personality disorder: An fMRI study. J Psychiatry Neurosci 38:164–172.
67. Jacob GA, Gutz L, Bader K, Lieb K, Tüscher O, Stahl C (2010): Impulsivity in borderline personality disorder: Impairment in self-report measures, but not behavioral inhibition. Psychopathology 43:180–188.
68. van Eijk J, Sebastian A, Krause-Utz A, Cackowski S, Demirakca T, Biedermann SV, *et al.* (2015): Women with borderline personality disorder do not show altered BOLD responses during response inhibition. Psychiatry Res Neuroimaging 234:378–389.
69. Ruchsow M, Groen G, Kiefer M, Buchheim A, Walter H, Martius P, *et al.* (2008): Response inhibition in borderline personality disorder: Event-related potentials in a go/nogo task. J Neural Transm (Vienna) 115:127–133.
70. Kunert HJ, Druecke HW, Sass H, Herpertz SC (2003): Frontal lobe dysfunctions in borderline personality disorder? Neuropsychological findings. J Pers Disord 17:497–509.
71. Dinn WM, Harris CL, Aycicegi A, Greene PB, Kirkley SM, Reilly C (2004): Neurocognitive function in borderline personality disorder. Prog Neuropsychopharmacol Biol Psychiatry 28:329–341.
72. Ruocco AC, Laporte L, Russell J, Guttman H, Paris J (2012): Response inhibition deficits in unaffected first-degree relatives of patients with borderline personality disorder. Neuropsychology 26:473–482.
73. Hagenhoff M, Franzen N, Koppe G, Baer N, Scheibel N, Sammer G, *et al.* (2013): Executive functions in borderline personality disorder. Psychiatry Res 210:224–231.