Contrasting Emotion Processing and Executive Functioning in Attention-Deficit/Hyperactivity Disorder and Bipolar Disorder

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Attention-deficit/hyperactivity disorder (ADHD) and bipolar disorder (BD) are highly comorbid and share executive function and emotion processing deficits, complicating diagnoses despite distinct clinical features. We compared performance on an oculomotor task that assessed these processes to capture subtle differences between ADHD and BD. The interaction between emotion processing and executive functioning may be informative because, although these processes overlap anatomically, certain regions that are compromised in each network are different in ADHD and BD. Adults, aged 18–62, with ADHD (n = 22), BD (n = 20), and healthy controls (n = 21) performed an interleaved pro- and antisaccade task (looking toward vs. looking away from a visual target, respectively). Task irrelevant emotional faces (fear, happy, sad, neutral) were presented on a subset of trials either before or with the target. The ADHD group made more direction errors (looked in the wrong direction) than controls. Presentation of negatively valenced (fear, sad) and ambiguous (neutral) emotional faces increased saccadic reaction time in BD only compared to controls, whereas longer presentation of sad faces modestly increased group differences. The antisaccade task differentiated ADHD from controls. Emotional processing further impaired processing speed in BD. We propose that the dorsolateral prefrontal cortex is critical in both processing systems, but the inhibitory signal this region generates is impacted by dysfunction in the emotion processing network, possibly at the orbitofrontal cortex, in BD. These results suggest there are differences in how emotion processing and executive functioning interact, which could be utilized to improve diagnostic specificity.

Keywords: antisaccade, eye movements, executive functioning
BD typically presents later in life and is a disorder of emotion regulation and processing (APA, 2000; Townsend & Altshuler, 2012). Functionally, BD patients are slower to label emotions and require stronger emotional valence to label them accurately (Leppänen, 2006; Van Rheenen & Rossell, 2014a). Indeed, electrophysiological studies of face perception and emotion discrimination have demonstrated that neural activity begins within 170–200 ms (Degabriele, Lagopoulos, & Malhi, 2011; Eimer & Holmes, 2002; Rossion & Caharel, 2011), but individuals with BD have been shown to have longer latencies when presented with negatively valenced stimuli (Degabriele et al., 2011). Similarly, other groups have described consistent behavioral biases toward negative and ambiguous emotional stimuli in BD patients, but it is unclear if these deficits are due to an inability to discriminate between or label emotions (Dermietzel, Kryspin-Exner, Hasmann, & Dobmeyer, 2009; Henry et al., 2012; Van Rheenen & Rossell, 2014a; Vederman et al., 2012).

Cognitive and emotional deficits are not exclusive to each disorder (Walshaw, Alloy, & Sabb, 2010). Executive dysfunction of working memory, response inhibition, response flexibility, and set-shifting has been reported in BD (Goldberg & Chengappa, 2009; Torralva et al., 2011). ADHD patients, on the other hand, struggle to accurately perceive and identify emotional expressions regardless of medical treatment or emotional intensity, although this may be due to inattention to salient facial cues during encoding (Ibáñez et al., 2011; Uekermann et al., 2010). Interestingly, research in healthy aging (Uekermann, Channon, & Daum, 2006), depression (Uekermann, Abdel-Hamid, Lehmköper, Vollm, & Daum, 2008), and ADHD (Uekermann et al., 2010) has shown that executive functions are involved in resolving complex emotional information, which may explain the similar deficits observed in ADHD and BD. Indeed, there is substantial anatomical overlap between executive functioning and emotion processing networks, primarily in the basal ganglia and the DLPFC (McKenna & Eyler, 2012; Munoz, Armstrong, & Coe, 2007; Sweeney, Luna, Keedy, McDowell, & Clementz, 2007).

However, adults with ADHD and BD are rarely compared directly in terms of higher level cognitive functioning (Torralva et al., 2011), making it unclear whether or not there are differences between these disorders in executive functioning and emotion processing domains. Because both groups have been reported to have similar executive function deficits independently (Brown, 2008; Faraone et al., 2000; Goldberg & Chengappa, 2009; Torralva et al., 2011), it is possible that ADHD and BD would not differ on traditional tests of executive functioning when compared directly. However, other cognitive processes like emotion processing may be a differentiating factor between ADHD and a mood disorder such as BD when engaged with executive functioning systems on the same task, because emotion processing deficits in ADHD may be related to inattentiveness rather than emotion processing dysfunction itself (Ibáñez et al., 2011; Uekermann et al., 2010). Furthermore, assessing the interaction between cognitive and emotion processing systems in these populations may provide increased sensitivity that is lacking from traditional tests of executive functioning (Wasserman & Wasserman, 2012), by engaging structures related to emotion processing, like the OFC (Phillips, Ladouceur, & Drevets, 2008; Townsend & Altshuler, 2012; Versace et al., 2010), that are differentially compromised in ADHD and BD (Torralva et al., 2012; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005).

The antisaccade task is an example of an oculomotor task that assesses executive functions like response inhibition and processing speed via voluntary eye movements. The task requires inhibition of a prepotent saccadic response toward a visual target (pro-saccade) to instead look in the opposite direction (antisaccade; Munoz & Everling, 2004). Longer saccadic RTs (SRT; time from peripheral target onset to saccade initiation) and increased direction error rates (i.e., looking at a peripheral target when cued to look away) have been observed in BD and ADHD, whereas increased variability in SRTs (as measured by the coefficient of variation \[CV = SD/\text{mean}\]) has been observed in ADHD only (García-Blanco, Perea, & Salmerón, 2013; Harkvoort Schwedt, et al., 2013; Mueller et al., 2010; Munoz, Armstrong, Hampton, & Moore, 2003; O’Driscoll et al., 2005). Direction errors are indicative of response inhibition difficulties because executive control fails to prevent an automatic saccade toward the visual target. SRT indexes processing speed and voluntary suppression via the difference in time between inhibiting the automatic, sensorimotor response and the generation of the voluntary, goal-directed eye movement. Finally, the SRT CV has been used as an indicator of inattentiveness and distractibility; the inability to focus on the target/task results in greater variation trial to trial and suboptimal RTs (Adams, Roberts, Milich, & Fillmore., 2011; Munoz et al., 2003). The antisaccade task can be used to collect large amounts of data quickly and easily, cause little to no discomfort to participants, and can be modified easily to incorporate a range of emotional stimuli, making this an efficient and effective system to assess dysfunction in a way that could be clinically useful.

The goal of this study is to objectively compare executive functioning and emotion processing in ADHD and BD to establish how these systems may differentially interact to cause dysfunction. We modify the antisaccade paradigm to include task-irrelevant emotional distracters (see Figure 1). We utilize a stimulus onset asynchrony (SOA) of these emotional stimuli to compare baseline trials, when emotional stimuli and target are presented simultaneously, to trials where emotional stimuli are presented 200 ms before the target onset, thereby allowing sufficient time for face and emotion processing to occur (Degabriele & Lagopoulos, 2012; Eimer & Holmes, 2002; Rossion & Caharel, 2011). We expect an interaction among task, onset, and group where increased processing time of faces on the antisaccade task will negatively affect performance of the BD group. We use a visual control (coffee pot) and faces to consider whether visual stimuli or faces modulate behavior rather than specific emotions. On standard antisaccade trials, we expect that ADHD and BD will differ from healthy controls but not from one another. A three-way interaction between task, image, and group is of primary interest; processing specific emotional faces is expected to have a detrimental effect exclusively on BD participants for our measures of interest on the more cognitively challenging antisaccade task. This would be limited to neutral or sad faces because of the ambiguous and negative emotional valence they convey, which are difficult for those with BD to process (Henry et al., 2012).
Participants

All experiments were approved by our institution’s Human Research Ethics Board and adhered to the Canadian Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans. Participants gave informed consent and were compensated for their time. Patients included 22 ADHD (mean age = 33.8, range: 18–58; 13 male) and 20 BD (mean age = 37.4, range: 19–61; 10 male) participants who were diagnosed and recruited from a psychiatric adult outpatient clinic by one psychiatrist (co-author A.M.) to ensure diagnostic consistency (see Table 1). To be eligible, patients had to meet DSM–IV criteria (APA, 2000) for either ADHD or BD, without a comorbid diagnosis of ADHD or BD. The BD patients were assessed clinically within a week of testing in order to confirm the absence of any potential mood episode (manic, hypomanic, depressive, or mixed) as per DSM–IV diagnostic criteria (APA, 2000). Controls (n = 21, mean age = 35.5, range: 19–62; 14 male) were recruited via newspaper advertisement and were screened for psychiatric symptoms on the MINI 5.0.0, a short neuropsychiatric diagnostic interview (Sheehan et al., 1998). Using G’Power (Faul, Erdfelder, Lang, & Buchner, 2007), an n of 66 participants would be required to observe a moderate effect (.4) with the appropriate statistical power (1–β = .80 as per Cohen, 1988). However, 2 BD participants and 1 control were lost because of missing demographic and/or clinical information, making this sample slightly underpowered. BD participants maintained pharmacological treatment (i.e., lithium) during testing, for ethical concerns and to ensure euthymic mood state. Subjects in the ADHD group refrained from taking stimulant medication on the day of testing and completed the experiment in the morning to reduce participant burden.

Experimental Protocol

An infrared, camera-based eye tracker (EyeLink 1000; SR Research Ltd., Toronto, Canada) recorded monocular (right) eye position at a sampling rate of 500Hz. Stimuli were presented on a 17-inch, 1440 × 900 pixel LCD display with a refresh rate of 60Hz. The infrared camera and illuminator were attached to the bottom of the screen and angled slightly upward for optimal tracking. The screen was adjusted so that participants’ faces were centrally located 55–60 cm away from the screen. Participants’ heads were unconstrained, so small amounts of head movement were tolerated. A 9-point array was used to calibrate and validate eye tracking.

Participants sat in a dark room in front of the display and were instructed to fixate on a central fixation point (FP; 42.35cd/m², 0.5° diameter) whose color indicated the task instruction (green FP: prosaccade; red FP: antisaccade). Emotional stimuli were selected (8 Caucasian faces, 4 male) from the Radboud Faces Database (Langner et al., 2010). Images were grayscale, normalized for intensity distribution, and aligned such that the eyes and nose of each image appeared in the same location relative to the FP. Control conditions included an object (coffee pot) and no image (black rectangle). All
Demographic Information for Age, Level of Education, Diagnostic Subtype, Age at Diagnosis, Comorbidities, and Current Treatment

| Table 1 |
|-----------------------|-----------------------|-----------------------|
| **ADHD**              | **BD**                | **Control**           |
| **n (male)**          | **n (male)**          | **n (male)**          |
| 22 (13)               | 20 (10)               | 21 (14)               |
| **Age (SD)**          | **Age (SD)**          | **Age (SD)**          |
| 33.77 (11.59)         | 37.4 (13.64)          | 35.48 (11.75)         |
| **Level of education (n)** | **Level of education (n)** | **Level of education (n)** |
| High school (6), College (11), Undergraduate (5) | High school (4), College (5), Undergraduate (10), Graduate/professional (1) | N/A |
| **Diagnosis subtype (n)** | **Diagnosis subtype (n)** | **Diagnosis subtype (n)** |
| Combined (15), Inattentive (5), Impulsive (2) | Bipolar I (8), Bipolar II (12) | N/A |
| **Average age at diagnosis (SD)** | **Average age at diagnosis (SD)** | **Average age at diagnosis (SD)** |
| 30.45 (12.95)         | 31.2 (10.22)          | N/A                   |
| **Comorbidities (n)** | **Comorbidities (n)** | **Comorbidities (n)** |
| None (13), MDD (5), GAD (3), SUD (1), ODD (1), Trichotillomania (1), Impulse control disorder (6), Anxyolitic (1) | None (12), SUD (3), GAD (2), BD (1), ODD (1), Mood stabilizer (2), Antipsychotic (14), Stimulant (1) | None (21) |
| **Current treatment (n)** | **Current treatment (n)** | **Current treatment (n)** |
| Stimulant (21), Mood stabilizer (2), Anxyolitic (2) | Mood stabilizer (2), Antipsychotic (14), Stimulant (1) | N/A |

Note: *ADHD = attention-deficit/hyperactivity disorder; BD = bipolar disorder patients; n = sample size; SD = standard deviation; MDD = major depressive disorder; GAD = generalized anxiety disorder; SUD = substance use disorder; ODD = oppositional defiant disorder; BD = bipolar disorder; ODD = oppositional defiant disorder; Psychosis-NOS = psychosis not-otherwise-specified; OCD = obsessive-compulsive disorder.*

Each trial (Figure 1A) began with presentation of the central FP for a randomized period of time (500–900 ms). Emotional and control stimuli were displayed directly behind the FP either 200 ms before or simultaneously with the appearance of the peripheral target. We defined this epoch between stimulus appearance and target appearance as the SOA. After the peripheral target was presented, all stimuli remained on the screen for 1000 ms. The screen then went black for 500 ms before the next trial began. “No image” trials only had the FP visible until the target appeared. In total, participants completed 512 randomly interleaved pro and antisaccade trials, with breaks every 32 trials for participant’s comfort or to recalibrate the eye tracking system. Of the 512 trials, 256 were presented with an emotional face (64 trials per emotion) and 256 for control conditions (128 for the object, 128 for no image conditions). Trials were evenly split between pro and antisaccade trials and whether the peripheral target was presented to the left or right.

**Data Analysis**

Each trial and eye movement was categorized by an automarking script written in MATLAB 7.4 (The MathWorks Inc., Natick, MA) and was manually verified by one coauthor (S.S.) to ensure accuracy and consistency. Eye movements were identified across 3 sampling points of instantaneous speed on a trial-by-trial basis. The eye movement was considered a saccade when these sample points were 1.5 standard deviations from the speed of background noise and the amplitude of the movement was >2° in the horizontal direction. Trials were excluded (2.5% of all trials removed; 2.6% ADHD trials, 4.2% BD trials, 0.7% control trials) if eye tracking was lost (i.e., blinking during a trial) or if there was no saccade. Dependent measures of interest included direction errors and SRT (Figure 1A, 1C). Direction errors were defined as saccades that followed the wrong instruction. To be considered a direction error, the saccade had to have an instantaneous speed 1.5 standard deviations above background noise in the wrong direction (i.e., an eye movement toward the peripheral target instead of away on an antisaccade trial). SRT refers to the time from peripheral target appearance to the initiation of the correct saccade. Both direction error percentage and SRT were calculated as per-subject averages, which were then used in the following analyses to compare across groups. Each participant group showed a high amount of SRT variability, prompting us to also consider the CV for SRT across groups as a third dependent variable.

Initially, demographic variables, such as age at diagnosis and education level, were compared between groups with a one-way ANOVA, whereas correlations between these demographic variables and two of our dependent variables of interest, SRT and direction error percentage, were also considered to establish appropriate covariates. Education level and age were ultimately used as covariates for the following analysis of covariance (ANCOVA) analyses. Next, nonparametric Kolmogorov–Smirnov tests were
run to compare the SRT and direction error distributions between groups. Then, mixed, repeated measures omnibus ANCOVAs were run in SPSS 22 (SPSS IBM, New York, NY) with four independent variables: group (ADHD, BD, control), task (prosaccade, antisaccade), SOA (0 ms, 200 ms), and image (fear, happy, sad, neutral, object). In each ANCOVA, participant group was the between-subjects variable, whereas all others were within-subject. The first omnibus ANCOVA considered effects of the pro and antisaccade trials without any visual stimuli (no image trials), and was run separately as a baseline comparison of executive function. SOA was collapsed because processing effects would not be possible because there was no visual distractor; therefore, the initial omnibus ANCOVA had a $3 \times 2$ design (participant group by task). The second omnibus ANCOVA was run with a $3 \times 2 \times 2 \times 5$ design (participant group, task, SOA, image) to assess interactions between the various image types and their onset on participant group. The final omnibus ANCOVA was run with a $3 \times 2 \times 2$ design to assess face processing effects by collapsing across emotions. Any 3-way interactions found in the omnibus ANCOVAs were further analyzed by 2-way ANCOVAs. If interactions were still significant after the 2-way ACV analysis, post hoc tests were reported: The Tukey’s HSD test was used when variance was equal, and the Dunnett T3 when unequal. Partial eta square effect sizes are reported for the interactions that are described while Cohen’s pooled $d$ scores are reported for specific group differences.

**Results**

**Demographic Differences**

A one-way ANOVA demonstrated there were no differences between groups for age, gender, or age at diagnosis ($F(2, 60) = .444, p = .644$; $F(2, 60) = .610, p = .547$; $F(1, 40) = .013, p = .909$, respectively; Table 1). However, differences were found for education level between ADHD and controls ($F(2, 60) = 3.568, p = .034$; Bonferroni $p = .044$), which, despite being typical of ADHD (Frazier, Youngstrom, Glutting, & Watkins, 2007), affects performance on the antisaccade task (Evdokimidis et al., 2002). Surprisingly, correlations were not found in the ADHD group, but in the BD group. The BD group correlations were between education level and direction error percentage for fearful ($r = -.661, p = .002$) and sad ($r = -.478, p = .033$) prosaccade trials and between education level and SRT on prosaccade object trials ($r = -.454, p = .044$). In spite of these findings, follow up repeated measures ANOVA analyses did not reveal any main effects or interactions involving education level. Therefore, education level was not of interest as an independent variable and was therefore used as a covariate in the following analyses.

Age was also used as a covariate because behavior on the pro/antisaccade task varies with age (Alahyane, Brien, Coe, Stroman, & Munoz, 2014; Munoz, Armstrong, & Coe, 1998) and it correlated with our dependent variables, as expected. Direction errors and age only correlated within the ADHD group. Direction errors correlated with age for both standard prosaccade ($r = .512, p = .015$) and antisaccade ($r = .429, p = .046$) trials. Fearful faces on prosaccade trials ($r = .607, p = .003$) and sad faces on antisaccade trials ($r = .465, p = .029$) also had significant correlations between direction error percentage and age. On the other hand, SRT correlated with age on prosaccade no-image trials for ADHD ($r = .608, p = .005$), BD ($r = .45, p = .046$), and controls ($r = .6, p = .004$). SRTs on antisaccade trials with no image also significantly correlated with age for ADHD ($r = .528, p = .012$) and BD ($r = .44, p = .05$) participants. SRTs for fearful, happy, sad, neutral, and object prosaccade ($r = .574, p = .005$; $r = .582, p = .004$; $r = .605, p = .003$; $r = .472, p = .026$; $r = .576, p = .005$, respectively) and antisaccade ($r = .624, p = .002$; $r = .578, p = .005$; $r = .606, p = .003$; $r = .586, p = .004$; $r = .571, p = .005$, respectively) trials correlated with age in the ADHD group. Similarly, SRTs for fearful, happy, sad, neutral, and object prosaccade ($r = .528, p = .014$; $r = .562, p = .008$; $r = .482, p = .027$; $r = .492, p = .023$; $r = .572, p = .007$, respectively) and antisaccade ($r = .557, p = .009$; $r = .579, p = .006$; $r = .506, p = .019$; $r = .519, p = .016$; $r = .524, p = .014$, respectively) trials correlated with age in the control group. Finally, the BD group showed correlations between age and SRT on fearful prosaccade ($r = .493, p = .027$) trials only and on happy ($r = .575, p = .008$), neutral ($r = .444, p = .05$), and object ($r = .477, p = .034$) antisaccade trials.

In the ADHD group, age at diagnosis correlated with direction error percentage for standard prosaccade ($r = .542, p = .011$) and antisaccade ($r = .465, p = .034$) trials. In addition, direction error percentage correlated with age at diagnosis on fearful prosaccade trials ($r = .67, p = .001$) and on happy ($r = .528, p = .014$), and sad ($r = .485, p = .026$) antisaccade trials in the ADHD group. Age at diagnosis also correlated with SRT in the ADHD group on standard prosaccade ($r = .526, p = .014$) and antisaccade ($r = .472, p = .031$) trials, in addition to fearful ($r = .471, p = .031$) and object ($r = .45, p = .047$) antisaccade trials. However, these correlations were not found in the BD group, nor were differences found between the patient groups when compared in the one-way ANOVA described above. We felt that utilizing age at diagnosis as a covariate would remove variance that would be attributed to those with the most severe forms of psychopathology, so this demographic variable was not used as a covariate or independent variable in any of the following analyses despite these significant correlations.

**Basic Pro- and Antisaccade Behavior**

We first established baseline performance on pro/antisaccade tasks for these groups by analyzing trials when no image was presented. We expected similar levels of dysfunction in both ADHD and BD because of similarities in executive deficits that have been observed when these groups have been studied in isolation (Brown, 2008; Faraone et al., 2000; Goldberg & Chen-gappa, 2009; Torralva et al., 2011). The proportion of group responses over time demonstrated that, on prosaccade trials (Figure 2A), ADHD and BD were virtually identical; both groups were marginally slower and made slightly more direction errors than controls, but differences in these distributions were not significant as per Kolmogorov–Smirnov tests. When considering antisaccade trials (Figure 2B), all groups had longer SRTs and more direction errors compared to prosaccade trials, and in general, the patient groups performed worse than controls. The patient group distributions did not differ from one another for either direction error percentage or SRT. However, Kolmogorov–Smirnov tests showed
that the distribution of direction errors differed between BD and controls on antisaccade trials ($p = .024$), which is indicated by the vertical shift in distributions in Figure 2B. Similarly, SRT distributions on antisaccade trials differed between ADHD and control participants ($p = .034$), whereas the BD distribution trended toward a significant difference from controls ($p = .067$) in this condition. This effect is indicated by the horizontal shift of the cumulative distributions (i.e., exemplary epoch inset in Figure 2B).

**Direction errors.** The omnibus ANCOVA revealed a task by group interaction for direction error percentage ($F(2, 58) = 3.849$, $p = .027$, $\eta^2_p = .117$) only. Post hoc tests of the task by group interaction revealed that ADHD (m = 14.4%, SD = 9.6%, SEM = 1.2%) participants made significantly more errors than controls (m = 7.2%, SD = 7.6%, SEM = .9%) in the antisaccade condition (Figure 3A; $p = .027$, $d_p = .832$). In addition, the BD (m = 16.7%, SD = 16.8%, SEM = 2.1%) versus control comparison was trending toward significance ($p = .084$, $d_p = .725$) despite a higher mean error rate in the BD group than the ADHD group in the antisaccade condition. The lack of a significant difference between BD and controls with regard to direction errors is likely due to a high level of variance in the BD group.

**Saccadic reaction time.** Only a main effect of task ($F(2, 58) = 8.449$, $p = .005$, $\eta^2_p = .127$) was revealed by the omnibus ANCOVA for SRT. Pairwise comparisons of the task main effect showed increased SRT in the antisaccade condition (m = 321.0 ms, SD = 69.8 ms, SEM = 8.8 ms) relative to the prosaccade condition (m = 261.8 ms, SD = 63.2 ms, SEM = 8.0 ms; $p = .005$).

The omnibus SRT CV ANCOVA revealed a main effect of group ($F(2, 58) = 6.826$, $p = .002$, $\eta^2_p = .191$); both ADHD (m = 31 ms, SD = 8.4 ms, SEM = 1.8 ms; $p = .039$) and BD (m = 33.3 ms, SD = 8.1 ms, SEM = 1.8 ms; $p = .002$) groups were more variable than controls (m = 23.7 ms, SD = 14.0, SEM = 1.8 ms) regardless of prosaccade or antisaccade condition. In addition, a task by group interaction ($F(2, 58) = 4.668$, $p = .013$, $\eta^2_p = .139$) was found. Post hoc comparisons revealed that the ADHD group had more variable SRTs than the control group on both prosaccade (ADHD m = 34.4 ms, SD = 11.0 ms, SEM = 1.4 ms; control m = 26.5 ms, SD = 7.3 ms, SEM = .9 ms; $p = .024$, $d_p = .845$) and antisaccade (ADHD m = 28.1 ms, SD = 9.0 ms, SEM = 1.1 ms; control m = 21.8 ms, SD = 6.1 ms, SEM = .8; $p = .023$, $d_p = .816$) trials. The BD group only differed from controls on prosaccade trials (BD m = 39.6 ms, SD = 12.8 ms, SEM = 1.6 ms; $p = .001$, $d_p = 1.265$). The patient groups did not differ from one another with regard to SRT CV.

**Emotion Processing Effects**

After establishing baseline performance on the pro- and antisaccade tasks, we considered how emotional stimuli may modulate behavior. We expected that, for the BD group, processing emotional stimuli on the more cognitively challenging antisaccade trials would have the greatest effect on behavior and this would be specific negative and ambiguous emotions (Degabriele et al., 2011; Derntl et al., 2009; Vederman et al., 2012). The Kolmogorov–Smirnov analyses that were run revealed emotion-specific effects on both direction error percentage and SRT, but these differences in distributions were limited to antisaccade trials only. First, the vertical shift seen in Figure 4B displays differences in direction error distributions between ADHD and controls to fearful ($p = .01$), neutral ($p = .025$), and object ($p = .026$) stimuli on antisaccade trials. On the other hand, BD direction error distributions differed from controls during fearful ($p = .03$), sad ($p = .001$), neutral ($p = .01$), and object ($p = .023$) conditions on antisaccade trials. Direction error distributions did not differ between patient groups. With regard to SRT distributions, the ADHD distributions differed from controls...
Figure 3. Comparisons of our dependent measures of interest by task type with no image. (A) Percentage of trials that were incorrect (i.e., looking toward the target on an antisaccade trial). (B) Mean saccadic RT for correct pro and antisaccades for each group. CTRL = controls; BD = bipolar disorder patients; ADHD = attention-deficit/hyperactivity disorder participants. # indicates 0.1 > p > .05, * indicates p < .05. Error bars represent standard error. See the online article for the color version of this figure.

when presented with neutral faces on antisaccade trials only (p = .036). The SRT distributions of the BD group differed from controls when presented with fearful (p = .021), sad (p = .023), and neutral (p = .01) faces, with a trending difference between BD and controls when presented with happy faces (p = .053) on antisaccade trials. SRT distributions did not differ between patient groups. The SRT differences are highlighted by the horizontal shifts in the distributions as highlighted in the exemplary epochs in the Figure 4B insets.

Direction errors. The direction error percentage omnibus ANCOVA revealed a main effect of participant group (F(2, 58) = 5.703, p = .005, η²_p = .164) and a task by group interaction (Figure 5; F(2, 58) = 4.717, p = .013, η²_p = .164). No other effects were significant. Pairwise comparisons showed that controls (m = 6.3%, SD = 10.8%, SEM = 1.4%) made less errors in general than both BD (m = 12.204%, SD = 10.945%, SEM = 1.4%, p = .01) and ADHD (m = 11.681, SD = 10.934, SEM = 1.4%, p = .027) participants. There was no effect of image and onset, so we collapsed across these conditions for follow-up post hoc tests for the task by group interaction. These post hoc tests showed that both BD (m = 21.9%, SD = 11.8%, SEM = 1.5%; p = .015, d_b = .907) and ADHD (m = 18.4%, SD = 11.8%, SEM = 1.5%; p = .017, d_b = .901) participants made more errors than controls (m = 10.2%, SD = 5.5%, SEM = .7%) on antisaccade trials. Here, as in Section 3.2.1, both patient groups made more direction errors relative to controls, but did not differ from one another.

Saccadic reaction time. The omnibus ANCOVA for SRT revealed a main effect of task (F(1, 58) = 7.05, p = .01, η²_p = .108): SRTs were slower on antisaccade versus prosaccade (p < .001) trials. However, two three-way interactions were significant. First, an interaction was found between task, image, and group (Figure 6; F(8, 58) = 2.607, p = .013, η²_p = .082). To better interpret the three-way interaction, we conducted a two-ANCOVA for the task by group interactions for each emotion independently. Sad (F(2, 58) = 4.309, p = .018, η²_p = .057, p2 = .089) and neutral (F(2, 58) = 3.64, p = .032, η²_p = .112) faces showed significant task by diagnosis interactions, whereas fearful faces were trending toward significance (F(2, 58) = 2.877, p = .064, η²_p = .09). Post hoc tests revealed that BD participants had longer SRTs than did controls for fearful (BD m = 326.6 ms, SD = 77.8 ms, SEM = 9.8 ms; control m = 274.3 ms, SD = 63.2 ms, SEM = 8.0 ms; p = .044, d_b = .74), sad (BD m = 324.7 ms, SD = 77.2 ms, SEM = 9.7 ms; control m = 272.9 ms, SD = 63.8 ms, SEM = 8.0 ms; p = .053, d_b = .734), and neutral (BD m = 339.3 ms, SD = 72.9 ms, SEM = 9.2 ms; control m = 270.4 ms, SD = 63.6 ms, SEM = 8.0 ms; p = .003, d_b = 1.01) faces on antisaccade trials. The ADHD group did not differ from the BD or control groups in any condition. Second, an interaction between SOA, image, and group (F(8, 58) = 2.115, p = .044, η²_p = .068) was found. With regard to the SOA, image, and group three-way interaction, only sad faces (F(2, 58) = 4.358, p = .017, η²_p = .131) showed an onset by group interaction in the follow-up two-way ANCOVA. However, post hoc testing did not reveal any significant group differences beyond a slight increase in SRT for BD relative to controls (BD m = 270.4 ms, SD = 64.2 ms, SEM = 8.1 ms; control m = 228.5 ms, SD = 62.7 ms, SEM = 7.9 ms; p = .105, d_b = .661) in the 200-ms condition.

When considering the effects emotional stimuli had on the coefficient of variation for SRT between our groups, only main effects of onset (F(2, 58) = 7.006, p = .01, η²_p = .108) and group (F(2, 58) = 7.195, p = .002, η²_p = .199) were found. The 200-ms SOA (m = 28.9 ms, SD = 6.1 ms, SEM = .8 ms) resulted in increased variability compared to the 0-ms SOA (m = 26.7 ms, SD = 6.1 ms, SEM = .8 ms; p = .002), whereas both ADHD (m = 29.9, SD = 9.6 ms, SEM = 1.2 ms; p = .004) and BD (m = 29.5, SD = 9.8 ms, SEM = 1.2 ms; p = .007) participants were more variable than controls (m = 24.1 ms, SD = 9.6 ms, SEM = 1.2 ms) in general, demonstrating increased variability of the patient groups irrespective of image or task.

Face Effect Analysis

To confirm that the effects described above were due to emotion processing deficits as opposed to face processing deficits, we collapsed across emotions and compared the resulting “face” condition to the object control condition. The omnibus ANCOVA revealed main effects of group (F(2, 58) = 4.938, p = .01, η²_p = .143) and task (F(1, 58) = 5.625, p = .021, η²_p = .087), and a task by group interaction (F(2, 58) = 4.568, p = .014, η²_p = .134) for direction errors. Neither the image, task, group interaction (F(4, 58) = .891, p = .471, η²_p = .029) nor the image, SOA, group interaction (F(4, 58) = .33, p = .857, η²_p = .011) were significant. This pattern of results was consistent across all analyses.
For SRT, main effects of task ($F(1, 58) = 19.353, p < .001, \eta^2 = .253$), group ($F(2, 58) = 3.365, p = .04, \eta^2 = .104$), and SOA ($F(1, 58) = 6.46, p = .026, \eta^2 = .081$) were significant in the omnibus ANCOVA. However, the three-way interactions of interest—task, image, and group ($F(2, 58) = 3.609, p = .042, \eta^2 = .101$) and SOA, image, and group ($F(2, 58) = 2.95, p = .06, \eta^2 = .091$) interactions—were not significant. Averaging across emotions and using faces only eliminated the emotion-specific differences between BD and controls we originally observed.

Subsample Analysis

The sample used here had a variety of comorbidities, including major depressive disorder in the ADHD population, which may have influenced behavioral performance when presented with emotional stimuli. In order to assess whether any of the effects described previously were driven by these comorbidities, we ran the same set of analyses with participants who had no comorbid psychiatric diagnosis. Ultimately, 13 ADHD, 12 BD, and 22 control participants were used in this subsample analysis. On pro/antisaccade trials with no image, a main effect of group ($F(2, 41) = 3.953, p = .027, \eta^2 = .162$) and a task by group interaction ($F(2, 41) = 4.164, p = .023, \eta^2 = .169$) were found with regard to direction errors from the omnibus ANCOVA. Post hoc testing of the task by group interaction showed that the ADHD group made more errors than controls ($p = .025$) only. The SRT omnibus ANCOVA revealed a main effect of group ($F(2, 41) = 5.797, p = .021, \eta^2 = .124$). Finally, the SRT CV omnibus ANCOVA showed a task by group interaction ($F(2, 41) = 3.823, p = .03, \eta^2 = .157$), where the BD group was more variable than controls ($p < .001$) and ADHD trended toward increased variability from controls ($p = .051$) on prosaccade trials.

When considering trials with emotional stimuli, only a main effect of group was found from the direction error omnibus ANCOVA ($F(2, 41) = 5.425, p = .008, \eta^2 = .209$). On the other hand, main effects of group ($F(2, 41) = 3.44, p = .042, \eta^2 = .144$) and task ($F(2, 41) = 4.017, p = .051, \eta^2 = .089$) were found with
regard to the SRT omnibus ANCOVA. The task, image, and group three-way interaction also remained significant for SRT ($F(8, 41) = 2.969, p = .004, \eta_p^2 = .127$), and task by group interactions were maintained for fearful ($F(2, 41) = 4.241, p = .046, \eta_p^2 = .094$) and sad ($F(2, 41) = 5.259, p = .009, \eta_p^2 = .204$) faces in the follow-up two-way ANCOVA. Finally, group ($F(2, 41) = 7.285, p = .002, \eta_p^2 = .262$) and SOA ($F(1, 41) = 5.298, p = .027, \eta_p^2 = .114$) main effects were also significant from the SRT CV omnibus ANCOVA.

Although underpowered, this analysis mirrors the results described above, differing only with regard to the effect of neutral faces on SRT ($F(2, 41) = 2.507, p = .094, \eta_p^2 = .109$) in the task, image, and group interaction and the SOA, image, and group interaction itself ($F(8, 41) = .71, p = .682, \eta_p^2 = .033$), which were no longer significant.

**Discussion**

The goal of this study was to compare executive functioning deficits between ADHD and BD using an oculomotor paradigm and assess how emotion processing modulated these behavioral responses in a diagnosis-specific manner. We found in the standard antisaccade task that direction errors best differentiated the ADHD group from controls, whereas higher error rates subtly differed between BD and controls. However, the variation of SRT differed between groups: Both ADHD and BD groups had increased variability SRT on prosaccade trials compared to controls, whereas only the ADHD group had increased variability in SRT on antisaccade trials relative to controls as well. Importantly, we found that incorporating emotional faces as task-irrelevant distracters exacerbated SRT differences between BD and controls, suggesting an interaction that was exclusive to BD when cognitive and emotional processing systems were engaged simultaneously.

**Executive Functioning**

Executive functioning includes a variety of specific processes that are integral to higher order cognition, including response inhibition, which is well established as a critical component within executive control systems (Torralva et al., 2011; Walsh et al., 2010). On pro/antisaccade tasks, BD and ADHD participants typically have response inhibition difficulties, and can have highly variable and longer response times (Garcia-Blanco et al., 2013; Harkvoort-Schwerdtferger et al., 2013; Munoz et al., 2003), all

**Figure 5.** Mean direction errors across participant groups, collapsed across image type and onset. CTRL = controls; BD = bipolar disorder patients; ADHD = attention-deficit/hyperactivity disorder participants. * indicates $p < .05$. Error bars represent standard error. See the online article for the color version of this figure.

**Figure 6.** Mean saccadic RT (SRT) per participant group for each image presented on pro versus antisaccade tasks. CTRL = controls; BD = bipolar disorder patients; ADHD = attention-deficit/hyperactivity disorder participants. # indicates $0.1 > p > .05$, * indicates $p < .05$, ** indicates $p < .005$. Images with a significance star are those that had a significant two-way interaction (i.e., a group by task interaction was significant for Fearful faces). Error bars represent standard error. See the online article for the color version of this figure.
characteristics we have observed here. Direction errors were used as an index of response disinhibition because the automatic saccade toward the visual target on an antisaccade trial is a result of a failure in executive control (Munoz et al., 2007), which was observed in the ADHD group on standard antisaccade trials. Longer and more variable SRTs in the ADHD and BD groups were also found, which were our indices of processing speed and inattentiveness (Munoz et al., 2003, 2007). This is of particular interest because this is the first instance that ADHD and BD populations have been directly compared on an executive functioning oculomotor task. These results suggest that there may be certain commonalities in the pathophysiology between ADHD and BD that are specific to executive functions related to response disinhibition and inattentiveness. However, these results lacked specificity such that BD could not be differentiated from ADHD. The similarities in executive function deficits observed here and elsewhere between ADHD and BD (Torralva et al., 2011; Walshaw et al., 2010) could be built upon by incorporating another high-level cognitive system, like emotion processing, to capture potential differences between these disorders that may be seen clinically or in everyday life (Torralva et al., 2012).

Emotion Processing

Emotional and cognitive processes have been shown to correlate with one another, and it has been hypothesized that better developed emotional processes facilitate stronger self-control (Uekermann et al., 2008). We hypothesized that emotion processing may utilize cognitive resources that would otherwise support executive functioning during antisaccade trials, which would detrimentally affect the performance of the BD group specifically because this disorder is characterized by emotion processing deficits (Degabriele et al., 2011; Leppänen, 2006; Van Rheenen & Rossell, 2014a). Both direction error percentage and SRT variability did not seem to be modified by emotional processing. The relationship between emotion-specific effects and cognitive processing was limited to processing speed on the antisaccade task in the BD group only.

Slower inhibitory responses in BD were observed here and have been found on the antisaccade tasks across all mood states previously (García-Blanco et al., 2013), suggesting that these effects are likely mood stable. However, participants in both of these studies were medicated, and this behavioral pattern must be assessed further in the absence of pharmacological treatment. Additionally, our findings show greater deficits when the BD group was presented with negatively valenced or ambiguous emotions. Deficits in emotion processing have been reported in the past when emotions are weakly valenced but lack consistency with regard to biases toward positively or negatively valenced stimuli (Leppänen, 2006; Van Rheenen & Rossell, 2014a). Our findings reinforce previous work suggesting a bias toward negative or ambiguous stimuli (Dennl et al., 2009; Getz, Shear, & Strakowski, 2003; Leppänen, 2006; Vederman et al., 2012). A benefit of our design was the ability to compare across two visual controls: one for any visual stimulus (coffee pot), and the other for faces (collapsing across emotions). We found that response disinhibition and variability were consistent across all conditions, whereas only processing speed was modulated by emotional stimuli in the BD group.

This pattern of behavior seems to better encapsulate the everyday social difficulties BD patients face (Green, Cahill, & Malhi, 2007; Van Rheenen & Rossell, 2014b); Individuals interact with complex social-emotional stimuli while performing cognitively demanding tasks and are unable to complete them or process these stimuli appropriately (Cusi, Macqueen, & McKinnon, 2012). Emotion processing difficulties for the ADHD group were not observed with regard to SRT, suggesting that the interaction effect between executive functioning and emotion processing is specific to BD. However, we did notice qualitative similarities between the ADHD and BD groups when fearful faces were presented (Figure 4A). Fearful stimuli have been shown to increase error rates and processing speeds on behavioral tasks in ADHD in the past (Brotman et al., 2010; Dickstein & Castellanos, 2011). Fear processing may be distinct from other emotional processes or may be more vulnerable than other emotions in a broader emotion processing network in ADHD.

Anatomical Substrate

The antisaccade task highlights deficits of executive function, primarily because this task recruits cortical regions, such as the frontal, supplementary, and parietal eye fields, DLPFC, and regions of the basal ganglia (Munoz & Everling, 2004). These regions support functions like response inhibition, working memory, motor preparation, fixation control, motivation, and reward processing (Bari & Robbins, 2013; Corneil & Munoz, 2014; Ghahremani et al., 2012; Lindström & Bohlin, 2012; Phillips et al., 2008; Sweeney et al., 2007). Dysfunction in both BD and ADHD emotion processing networks involve similar structures in this frontostriatal circuit (Dickstein & Castellanos, 2011; Phillips et al., 2008), where atypical activity in the DLPFC, amygdala, and basal ganglia have been reported in both groups (Brotman et al., 2010; Ibáñez et al., 2011; Delvecchio, Sugranyes, & Frangou, 2013; Dickstein & Castellanos, 2011; Garrett et al., 2012; McKenna & Eyler, 2012). In addition, anterior cingulate (ACC) hyperactivity (Bush, 2011) has been reported in ADHD, whereas underactivation of cortical regions of top-down control, like the medial prefrontal cortex, OFC, and ACC, have been described in BD emotion processing networks previously (Delvecchio et al., 2013; Pavuluri, Passarotti, Harral, & Sweeney, 2009). Although speculation, the overlap between some of these regions may result in some of the similar behavioral deficits that have been observed in these groups in the past (Delvecchio et al., 2013; Ibáñez et al., 2011; García-Blanco et al., 2013; Hakvoort Schwertfeger et al., 2013; Torralva et al., 2011). There are some brain regions, such as the ACC and OFC, that are differentially impaired in ADHD and BD (Bush, 2011; Delvecchio et al., 2013; Pavuluri et al., 2009; Phillips et al., 2008) that may provide insight with regard to their pathophysiology.

The OFC in particular is involved in emotional control and has been shown to be reciprocally connected to the DLPFC, amygdala, and basal ganglia, making it a critical structure in mediating responses during emotion regulation and, perhaps unsurprisingly, has been reported as a locus of dysfunction in BD (Phillips et al., 2008). In the context of this study, we hypothesize that an interaction between emotion processing and executive functioning would be dependent on the role of the OFC: in this study, the DLPFC insufficiently suppresses both emotion processing and automatic oculomotor responses resulting in no emotion-specific changes when an error is made. However, the correct executive
control signal must be transmitted through the OFC to inhibit activation of subcortical limbic structures in order to make the correct eye movement, which is made more difficult for BD participants because of poor OFC functioning, thereby slowing down this groups’ responses on this task (Adler, DelBello, & Strakowski, 2006; Strakowski, Delbello, & Adler, 2005). The hypothetical relationships between these brain regions and the deficits we have observed must be elucidated further in future work.

Limitations and Future Directions

The results of the current study are promising, but emotional faces were task irrelevant, maintenance of treatment differed, mood state was not quantified, and the patient groups were fairly heterogeneous. These results provide a promising first step in capturing BD deficits to better differentiate this group from controls and show how dysfunction in emotion processing and cognitive domains for BD may differ from ADHD. Although we did not find any between-groups differences between the BD and ADHD groups, we do observe that despite similar deficits on the standard pro/antisaccade tasks, only the BD group was further impaired with the presentation of emotional faces. Therefore, better incorporation of emotional stimuli in the task may capitalize on these differences and exacerbate them between patient groups.

Second, there were differences in treatment maintenance between these groups. ADHD participants briefly discontinued stimulant treatment, whereas BD participants maintained pharmacological treatment because of ethical concerns. Stimulants have been shown to increase alertness, psychomotor speed, and RTs in general (Reilly, Lencer, Bishop, Keedy, & Sweeney, 2008), whereas antipsychotics have been shown to reduce error rates and result in faster RTs on the antisaccade task in schizophrenic patients (Harris, Reilly, Keshavan, & Sweeney, 2006). This may have affected our ability to detect differences between the patient populations: The ADHD group may be performing worse than if they continued treatment, and the BD group may be performing better because of their continued use of antipsychotics. Another possible limitation was the lack of a quantitative definition of euthymia, but such quantitative definitions have yet to be validated (Tohen et al., 2009). These definitions would be most critical in outcome studies, but for the scope of this project, a clinical assessment free of a significant mood episode as per DSM–IV criteria (APA, 2000) in advance of testing was sufficient to consider these participants as euthymic.

Finally, separating patient groups into subtypes (i.e., inattentive vs. hyperactive ADHD) may elucidate shared or distinct deficits that result in various disorder phenotypes. Our subsample analysis demonstrated that the results we have reported were consistent in participants who had no psychiatric comorbidities, but the effect of neutral faces was no longer significantly strong. It is worth mentioning that this subsample was underpowered, although the overall sample would have benefited from a larger sample size as well in order to draw more confident conclusions about these effects.

Conclusions

We compared executive functioning and emotion processing on an antisaccade task and were able to establish differences among ADHD, BD, and control groups. These effects are promising and provide a critical first step to address how these systems interact to cause dysfunction. Both ADHD and BD perform similarly on typical antisaccade trials, although only the ADHD group differed from controls, as the BD group was highly variable. Incorporating negative and ambiguous emotional faces increased dysfunction with regard to processing speed for BD participants. Further investigation may strengthen the notion that the interaction between these systems is different between BD and ADHD and can be used to better characterize each group in a clinically useful manner.

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