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Implicit Learning on a Probabilistic Classification Task in Adults and Adolescents with Bulimia Nervosa

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Abstract

Background—Dysfunction in frontostriatal circuits likely contributes to impaired regulatory control in Bulimia Nervosa (BN), resulting in binge-eating and purging behaviors that resemble maladaptive habits. Less is known about the implicit learning processes of these circuits, which may contribute to habit formation.

Methods—We compared 52 adolescent and adult females with BN to 55 healthy matched-controls during performance of a probabilistic classification learning task, one form of implicit learning. Groups were compared in accuracy and response times, using mixed-models with block, age, and diagnosis as predictors, corrected for multiple comparisons with confounds covaried.

Results—BN participants showed differences in performance on a probabilistic classification learning task that varied by age. Adolescents with BN initially performed as accurately as healthy adolescents, but showed poorer perseverance over time. Adults with BN initially performed less accurately than healthy adults, but improved to perform equivalently. Symptom severity was associated with poorer accuracy in both adults and adolescents with BN.

Conclusions—Frontostriatal dysfunction may underlie abnormalities in regulatory control and probabilistic classification learning in BN, likely contributing to the dysregulation of implicitly learned, maladaptive binge-eating and purging behaviors. Such dysfunction in BN may progress with increasing age, first manifesting in poor regulatory control over behaviors and then expanding to implicit learning processes that may underlie habitual behaviors.

Graphical Abstract

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Keywords

probabilistic classification learning; implicit learning; bulimia nervosa; weather prediction task; continuous performance task; self-regulation

1. Introduction

Bulimia Nervosa (BN) is characterized by the presence of recurrent episodes of binge eating that are associated with a sense of loss of control, followed by compensatory behaviors to counteract weight gain (American Psychiatric Association, 2013). These behaviors suggest the presence of self-regulatory control deficits likely due to a failure to engage frontostriatal systems appropriately (Marsh et al., 2011; Marsh et al., 2009b). While frontostriatal dysfunction and concomitant regulatory deficits are established in BN (Berner & Marsh, 2014), unknown is how these disturbances affect other functions that these circuits subserve, such as implicit learning.

Implicit learning, alternatively referred to as *procedural* or *habit learning*, occurs outside conscious awareness, and encompasses the acquisition of stimulus-response associations without recognition that learning is taking place. Implicit learning functions differently from declarative memory or action-outcome learning in which explicit awareness of stimulus-response associations drives responding, resulting in increased behavior when rewarded and decreased behavior when punished. Rather, implicitly-learned behavior develops gradually outside of awareness over time and many repetitions; as a result, the behavior becomes automated, relatively insensitive to reward, and highly resistant to change (Walsh, 2013). As such, individuals with BN may initially engage in binge-eating or purging behaviors because they produce rewards (i.e., praise for weight loss, pleasure from eating, or alleviation of negative affect). However, over time, repetition may allow them to become overtrained and habitual, a sort of “default” response that no longer requires reward and persists despite negative consequences (Walsh, 2013).

Findings from lesion studies indicate that implicit learning of automatic behaviors is supported by the striatum, a system that is both anatomically and functionally separate from the declarative learning system of the medial temporal lobe (Packard and Knowlton, 2002). In humans, implicit learning likely depends on parallel processing between the striatal implicit memory system and the medial temporal lobe explicit/associative memory systems, requiring adequate functioning of both subcortical systems alongside prefrontal regulatory mechanisms (McNamee et al., 2015). Frontostriatal dysfunction is implicated in disorders characterized by both regulatory disturbances and compulsive, repetitive behaviors (Marsh et

al., 2004; Marsh et al., 2009a; Steinglass and Walsh, 2006; Veltman et al., 2011). The automatic behaviors that characterize these disorders can be considered dysfunctional habits that escaped from prefrontal regulatory control. Likewise, the recurrent nature of the binge-purge cycle may represent maladaptive habit learning, wherein feeding behaviors are released from regulation and become compulsive in nature.

Probabilistic classification learning is one form of implicit learning in which cues are probabilistically associated with outcomes and participants process associations without explicit awareness. In the Weather Prediction Task (WPT), participants try to predict either “rain” or “shine” based on the presentation of cards whose cue-outcome associations vary probabilistically. Despite believing that they are simply guessing, healthy participants demonstrate above-chance ability to guess the correct outcome. In contrast, patients with diseases affecting frontostriatal circuitry (i.e., Parkinsons, Tourettes) demonstrate impaired performance, despite being able to adequately answer explicit questions about the task (Marsh et al., 2004); those who perform most poorly have documented frontostriatal abnormalities, deficits in regulatory capacity, and repetitive behaviors resembling habits (Kataoka et al., 2010, Leckman et al., 2014). As such, the WPT can be used to assess the functioning of the striatal-based implicit learning system in persons with BN.

Previous findings from adults diagnosed with Eating Disorder Not Otherwise Specified (EDNOS) suggested abnormal frontostriatal functioning during performance of the WPT (Celone et al., 2011). Although task performance was similar to healthy participants, those with sub-threshold BN symptoms demonstrated increased caudate and dorsolateral prefrontal cortex activation compared to healthy participants. Frontostriatal hyperactivity during implicit learning may compensate for inefficient circuit functioning in patients with bingeing and purging behaviors, consistent with previous findings of deficient frontostriatal functioning in patients with BN during tasks requiring regulatory control (Marsh et al., 2011; Marsh et al., 2009b). Together, these findings point to frontostriatal dysfunction in BN, but unknown is when differences in striatal-based implicit processes manifest or if they vary with severity.

To this end, we used the WPT to compare striatal-based implicit learning across a large sample of adolescents and adults with and without BN. Although performance differences were not detected in persons with subclinical-BN symptoms (Celone et al., 2011), we hypothesized that differences in performance would emerge when comparing a larger sample of adolescents and adults with full-syndrome BN to healthy matched-controls. In exploratory analyses, we also assessed whether severity of bulimic symptoms was associated with WPT performance. Finally, we compared BN and control groups in performance on tasks requiring the intact functioning of declarative memory and self-regulatory processes to assess whether any observed differences in WPT performance were specific to implicit processes or associated with both executive and implicit functions.

2. Methods

2.1. Participants

Data were acquired from 107 participants, who were either healthy controls (HC; $n=55$) or individuals with BN ($n=52$) recruited to participate in MRI studies of cognitive processes. All participants were females between the ages of 12–40; participants were classified as adolescents if aged 12–17 ($n=39$) and adults if aged 18+ ($n=68$). BN and HC groups did not differ in age, body mass index (BMI), or full-scale intelligence quotient (FSIQ). Participants with BN had an average illness duration of over four years and experienced significant symptomatology; 34% were currently taking SSRI medications (see Table 1).

All adults with BN met DSM-V criteria, whereas adolescents with BN were included if they experienced an average of one binge-eating episode (objective or subjective) and one purging episode per week for the past three months, with at least one binge-eating and purging episode occurring within the past month (Darcy et al., 2014). Exclusion criteria for all participants included history of neurological illness or head trauma, mental retardation or pervasive developmental disorder, or current substance disorder. HC participants and adults with BN were excluded for any current comorbid disorder; adolescents with BN were excluded only for comorbid disorders known to affect frontostriatal circuitry (i.e., ADHD, TS, OCD; Marsh et al., 2009). Five adults with BN (ages 18–21) were included despite having a current comorbid disorder because they were originally recruited as adolescents. Participants with BN with and without comorbidities did not differ in BMI, IQ, BN severity, or lifetime comorbid diagnoses.

BN and HC participants were recruited through advertisements, and group-matched by age, FSIQ, and BMI. Research was conducted in accordance with the Declaration of Helsinki and approved by the NYSPI Institutional Review Board. Written informed consent was obtained from adults and the parents of adolescent participants, and assent was obtained from adolescents. Participants were compensated for their time.

2.2. Procedure

2.2.1. Participant characterization—The *Structured Clinical Interview for DSM-IV Disorders* (18+; First et al., 2002) and *Kiddie Schedule for Affective Disorders and Schizophrenia* (<18; Kaufman et al., 1997) were administered. Severity of BN symptoms was assessed using the *Eating Disorder Examination* (Cooper and Fairburn, 1987). The *Beck Depression Inventory-II* (18+; Beck et al., 1996) and *Children's Depression Inventory* (<18; Kovacs, 1992) measured depressive symptoms. The *DuPaul-Barkley ADHD Rating Scale* (DuPaul, 1991) gauged inattention and hyperactivity symptoms, and the *Wechsler Abbreviated Scale of Intelligence* (Wechsler, 1981) estimated FSIQ.

2.2.2. Weather Prediction Task (WPT)—An abbreviated version of the WPT, with five blocks of 18 trials (total 90 trials), was selected to reduce participant burden. Although a longer 200-item version exists, the 90-item version has been successfully used with both youth and adults (Marsh et al., 2004), and as few as 10–20 trials have been shown to demonstrate probabilistic classification learning (Knowlton et al., 1994). Accuracy and

latency scores for each block were calculated by averaging within block. A one-minute break was provided after the first three blocks; instructions were identical before and after the break. On each trial, between 1–3 of four possible cue cards would appear vertically in one of fourteen combinations, and participants would predict rain or sunshine by selecting labeled keys. Combinations were randomized, with the restriction that identical combinations were not repeated sequentially and outcomes were not repeated more than five times in succession. Each outcome occurred equally often, and each cue was independently related to an outcome with a fixed probability (specific probabilities described elsewhere; Marsh et al., 2004). This probabilistic structure was used to minimize the likelihood that participants would gain explicit knowledge of associations. Feedback was provided, wherein a smiling face and bell were presented for correct responses and a frowning face and groan for incorrect responses. Responses were considered correct if selected outcomes were more strongly associated with the cue combinations appearing. However, because of the probabilistic design, a cue combination could sometimes be followed by the less-associated outcome; as such, participants could receive feedback that their response was incorrect even when scored as correct. Data were not included for trials where two outcomes were equally associated with the cue combination. Because the two outcomes occurred equally often, chance performance would be 50% and above-chance accuracy suggests probabilistic classification learning, a type of implicit learning. In healthy individuals, accuracy is consistently above chance (i.e., approximately 65–70%), whereas latency of response typically decreases across blocks (Gluck et al., 2002; Knowlton et al., 1994).

2.2.3. Declarative learning and memory tasks—Participants were administered a five-item, multiple-choice questionnaire assessing explicit knowledge of WPT cues, feedback, and procedures. Additionally, the WASI can also be considered an indirect measure of declarative memory (Cohen et al., 1997).

2.2.4. Self-regulatory control task—The Conners Continuous Performance Task (CPT; Conners, 1995) assesses inhibitory control, an aspect of self-regulation. The task rapidly presents letters, to which participants must respond with a button-press every time a letter except “X” is presented; they must refrain when “X” is displayed. Due to the high ratio of non-target to target letters, the task requires self-regulatory control to mobilize attentional resources and actively inhibit the automated response.

2.3. Analyses

Statistical analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC), using PROC MIXED linear mixed-model analysis with repeated measures across blocks and accuracy scores as the dependent variable. Analyses were performed for the whole sample and separately for adolescents and adults. For all models, diagnosis was a between-subjects factor and continuous age, BMI, duration of illness, and IQ were included as covariates. To model performance linearly, block was entered as an ordinal variable.¹ All 2- and 3-way interactions were examined, and insignificant interactions were removed via backwards stepwise regression with all models hierarchically well-formulated (i.e., all possible lower-

¹Quadratic and cubic functions were tested, but not supported.

order terms included; Morrell et al., 1997). Performance on the WPT was quantified by analyzing the percentage-correct (i.e., *accuracy*) across blocks. Hypothesized differences between groups were tested via significance of block-by-diagnosis interactions. All significance values were adjusted via modified-Bonferroni correction. Group differences in response time (i.e., *latency*) were assessed using identical mixed-modeling procedures but with latency scores as the dependent variable.

Pearson product-moment correlations were used to assess the significance of associations of accuracy and latency with IQ estimates (WASI) and duration of illness. Partial correlations were used to assess the significance of associations of accuracy and latency with the severity of BN symptoms (EDE), depressive symptoms (BDI or CDI), and ADHD symptoms (ADHD-RS), controlling for effects of age, BMI, IQ, and duration of illness. Comorbid depression and inattention-hyperactivity symptoms were included as covariates in all final models, and the effect of comorbid diagnoses was additionally assessed with separate models including only participants without comorbidities. Likewise, medication effects were assessed with separate models including only unmedicated BN participants. Independent t-tests were used to compare scores between groups on IQ, the WPT questionnaire, and the CPT. These group differences were explored to provide convergent evidence that differences in WPT performance were not due to group differences in overall IQ, explicit understanding of responses contingencies, or regulatory control necessary to persist in task performance.

3. Results

3.1. Accuracy

HC participants performed more accurately across time on the WPT than participants with BN, regardless of age ($F(4,438)=3.73, p < .01$). An age*block*diagnosis interaction was identified ($F(5,438)=3.85, p < .01$; see figure 1), wherein accuracy was relatively stable for both adolescent and adult HC participants, but varied for participants with BN by age. Adolescents with BN were initially as accurate as HC adolescents, but showed precipitous declines in accuracy in later blocks. Adults with BN initially performed less accurately, but gradually improved to levels commensurate with HC adults.

3.2. Latency

Analysis of latency scores across trials revealed a significant main effect of age ($F(1,444)=5.64, p < .01$), but no significant effect of diagnosis ($F(1,113)=0.71, p = 0.40$) or age*block*diagnosis interaction ($F(5,401)=1.45, p = 0.20$; see figure 2). Younger participants responded more rapidly than older participants, regardless of diagnosis.

3.3. Effects of symptom severity

Illness duration was not associated with accuracy or latency in the participants with BN (A: $r=0.02, p=.72$; L: $r=0.10, p=.46$) regardless of age (Adolescents–A: $r=0.06, p=.53$; L: $r=-0.17, p=.08$; Adults–A: $r=0.06, p=.42$; L: $r=0.11, p=.14$), suggesting that observed age*diagnosis interactions were not driven by expected associations between age and duration of illness.

Accuracy was inversely associated with the frequency of objective binge-eating ($r=-0.15$, $p < .05$) and vomiting ($r=-0.16$, $p < .01$) episodes, above and beyond the effects of age, BMI, duration of illness, or IQ. When examined separately, results were consistent in both adolescents and adults (Adolescents–V: $r=-0.27$, $p < .01$, OB: $r=-0.26$, $p < .01$; Adults–V: $r=-0.22$, $p < .01$, OB: $r=-0.29$, $p < .001$), indicating that participants with the most severe symptoms showed the poorest accuracy, regardless of age. Latency was not associated with symptom severity.

3.4. Effects of IQ, comorbid symptoms, and medication

IQ scores were not significantly associated with accuracy or latency in the BN group (A: $r=-0.13$, $p=.18$; L: $r=0.07$, $p=.24$) regardless of age (Adolescents–A: $r=-0.09$, $p=.66$; L: $r=-0.13$, $p=.56$; Adults–A: $r=-0.13$, $p=.43$; L: $r=0.27$, $p=.10$), suggesting that IQ did not drive group differences in performance on the WPT. Likewise, depressive symptoms were not associated with WPT accuracy ($r=0.01$, $p=.96$), but were positively associated with latency (i.e., depressed participants took slightly longer; $r=-0.11$, $p < .05$). Symptoms of inattention/hyperactivity were not associated with either accuracy or latency (A: $r=0.01$, $p=.89$; L: $r=0.08$, $p=.13$). Nevertheless, depression and ADHD symptoms were covaried in all final models.

Furthermore, there were no significant differences in accuracy or latency between BN participants with and without current (A: $F(1,60)=0.01$, $p=.98$; L: $F(1,60)=0.64$, $p=.43$) or lifetime (A: $F(1,60)=0.03$, $p=0.86$; L: $F(1,60)=0.02$, $p=0.91$) comorbid diagnoses. Comparing performance using only the HC participants and BN participants with no current or lifetime comorbid diagnoses still produced a significant age*block*diagnosis interaction ($F(5,359)=2.95$, $p < .01$), indicating that comorbid diagnoses did not contribute to our findings. Furthermore, neither accuracy or latency differed significantly between the BN participants with and without medications (A: $F(1,60)=0.59$, $p=.46$; L: $F(1,60)=0.67$, $p=.43$), and comparing performance across only the unmedicated BN and HC participants still produced a significant age*block*diagnosis interaction ($F(4,360)=2.36$, $p < .01$), suggesting that medication did not contribute to our findings. Lastly, BN participants with and without a history of AN did not differ significantly in accuracy ($F(1,58)=0.59$, $p=0.45$) or latency scores ($F(1,58)=0.77$, $p=0.39$), and comparing performance across only the HC participants and BN participants without a history of AN still produced a significant age*block*diagnosis interaction ($F(4,359)=2.87$, $p < .001$), further supporting the conclusion that differences in WPT performance are more likely due to BN than extraneous confounds.

3.5. Declarative memory and self-regulatory control measures

BN and HC participants did not differ in their scores on the WPT questionnaire ($M \pm SD$, $54.9\% \pm 11.5\%$ vs. $51.4\% \pm 10.4\%$; $F(1,36)=0.91$, $p=0.35$) or in IQ scores ($t(82)=0.06$, $p=0.95$), even when age, BMI, duration of illness, psychiatric symptoms, comorbid diagnoses, and medication use were included as covariates ($F(1,44)=1.80$, $p=0.15$). However, BN and HC participants did show significant differences in self-regulation on the CPT. Participants with BN made more commission errors, an error associated with impulsive responding ($F(1,484)=25.76$, $p < .001$), and omission errors, an error associated

with inattention ($F(1,484)=4.19, p < .05$). In addition, impulsive responding (i.e., commission errors) and inattention (i.e., omission errors) were inversely associated with accuracy on the WPT (C: $r=-0.11, p < .01$; O: $r=-0.11, p < .01$), controlling for relevant confounds. This deleterious influence of impulsive ($r=-0.20, p < .01$) and inattentive ($r=-0.13, p < .05$) responding was most pronounced in the adults with BN. In the adolescents with BN, sustained attention on the CPT was inversely associated with WPT accuracy ($r=-0.15, p < .05$), perhaps explaining their deterioration in performance over time.

4. Discussion

Compared to their healthy counterparts, participants with BN performed differently on the WPT, a probabilistic classification task that assesses a form of implicit learning and is therefore reliant on the intact functioning of frontostriatal circuits (Knowlton et al., 1996, McDonald and White, 1994). Adults with BN initially performed less accurately than control participants but eventually improved to equivalent levels by the final block. As such, adults with BN might retain the capacity for accurate implicit processing, but require more time to do so than healthy individuals. Alternatively, performance on the WPT was initially unaffected in adolescents with BN, who performed as accurately as their healthy counterparts in early blocks, but responded increasingly less accurately in later blocks. Across all ages, task accuracy was poorest in the BN participants with the most severe symptoms. These findings suggest that frontostriatal dysfunction may initially manifest as self-regulatory deficits in BN and then evolve into problems with implicit learning or processing in those with more severe symptoms.

Like implicit learning, *self-regulatory control* (one's capacity to organize and flexibly adapt thoughts, emotions, and behaviors in pursuit of broader goals; Marsh et al., 2009a) is subserved by overlapping frontostriatal circuits, with the dorsal striatum mediating action dependent on stimulus-response learning, ventral striatum mediating motivation and reward processing, and prefrontal components acting to organize, maintain, and switch cognitive-behavioral processes in accordance with goal pursuit (O'Doherty et al., 2004). Self-regulatory control is required to maintain attention and appropriate behavior, while inhibiting impulses toward immediate gratification when experiencing frustration, boredom, or distress during goal-directed behavior (Casey et al., 2011; Mischel et al., 1989). The capacity for self-regulation is a finite resource that can be temporarily fatigued, especially when the ability is underdeveloped or there are competing needs and demands (Casey et al., 2011; Mischel et al., 1989). While our correlation analyses preclude us from directly testing if regulatory capacity contributed to poor probabilistic classification task performance, many of the possible reasons for poor performance *could* be classified as regulatory failures: perhaps participants were fatigued, bored, or frustrated; no longer cared about completing the task well; were distracted by extraneous stimuli; or had exhausted their attentional abilities. Given that regulatory and implicit processes are supported by circuitry (O'Doherty et al., 2004), adolescents (and those with BN, in particular) may have experienced difficulty in later blocks of the WPT due to immature or exhausted self-regulatory capacity relative to adults. While only correlational, convergent evidence for this explanation is provided by associations between CPT and WPT performance scores.

Across both age groups, participants with BN performed less accurately on the WPT than control participants. Accuracy was significantly and inversely associated with the severity of BN symptoms in both adolescent and adult BN groups. While a correlation of symptom severity and task performance does not indicate that dysfunction in striatal-based implicit processing is the cause of maladaptive habitual behaviors in BN, it does suggest that dysfunction in this system may play a role in their neurobiological underpinnings. Associations of task performance with symptom severity remained even when important confounds were controlled.

Participants with BN were unimpaired on measures of declarative memory, suggesting that differences between groups in performance on the WPT were specific to implicit processes. The dissociation between explicit declarative memory and implicit learning systems are well-described by prominent computational model-free and model-based learning reinforcement learning theories (Sutton and Barto, 1998). Declarative memory tends to rely on model-based learning, involving relationships between stimuli encoded by the hippocampus and available to consciousness (Daw and Shohamy, 2008). Alternatively, implicit learning (of which probabilistic classification learning is one type) relies on a more model-free approach, wherein “trial and error” results in an implicit estimate maintained and updated based on reward prediction errors mediated by striatal dopaminergic activity (Glimcher, 2011). fMRI data supports the dissociation of these learning and memory systems, showing increased striatal and decreased medial temporal activations during performance of the WPT (Poldrack et al., 1999). Given their intact declarative memory function but noted differences in probabilistic classification, persons with BN may experience deficits in model-free learning or the interactions between model-based and model-free systems.

These noted differences in probabilistic classification likely reflect dysfunctional frontostriatal processes, consistent with those found in other populations with maladaptive repetitive behaviors (Marsh et al., 2009a, Veltman et al., 2011). Given these findings, the oft-used term “habit learning” as it applies to probabilistic classification tasks may be a misnomer, as individuals who experience maladaptive habit-like behaviors tend to perform poorly on the WPT. Task performance may not reflect the ability to learn implicitly or develop habits per se, but may instead index the ability to effectively *regulate* habits – that is, to flexibly respond to stimulus-response associations learned gradually and implicitly. As such, persons who rigidly adhere to certain behavioral repertoires may perform more poorly on the WPT due to poor regulatory control over habit-like behaviors, reflecting impaired frontostriatal functioning (Marsh, 2009; Marsh et al., 2011). Consistent with previous fMRI studies of frontostriatal dysfunction in BN (Marsh et al., 2011, Wagner et al., 2010), our findings suggest that circuit-based abnormalities may contribute to deficits in both regulatory and implicit functions in BN. Our findings further suggest that regulatory deficits may onset earlier in development, while differences in implicit learning processes may not manifest until adulthood (even when controlling for associations between age and duration of illness).

A possible limitation of this study was the use of the abbreviated WPT, which may not have provided sufficient opportunity to establish a stable learning curve. However, the 90-item

version has been successfully used in other studies with youth and adults (Marsh et al., 2004), and as few as 10–20 trials have demonstrated probabilistic classification learning (Knowlton et al., 1994). While it is possible that participants would have achieved greater accuracy if the task length had been doubled, in studies using the 200-trial version, accuracy typically increased to 60–70% within the first 20–50 trials and remained relatively stable thereafter (Gluck et al., 2002; Knowlton et al., 1994). Since the majority of gain is evident early, the decision was made to use the abbreviated version to reduce participant demand and fatigue. Future studies should explore the equivalencies of different forms of the WPT across healthy and clinical groups.

An additional limitation was the absence of a comparison group with impulsive or maladaptive repetitive behaviors who had healthy eating, which would allow examination of whether findings were specific to BN or indicative of a transdiagnostic propensity toward dysregulated behavior. A further limitation was the presence of comorbid illnesses and medication use in some participants with BN, particularly adolescents. However, this limitation was partially mitigated as findings remained significant even when statistically controlling for comorbid symptoms and excluding participants on medications and with current comorbidities. Supplemental analyses also explored whether history of any lifetime mental disorder influenced results, but no significant associations were found, further supporting the conclusion that differences in WPT performance were associated with BN and not other diagnoses.

Another limitation is that participants' motivation, fatigue, and other extraneous variables that may affect WPT performance were not measured directly. While performance on the CPT provides some correlational, convergent evidence for the role of regulatory deficits, other interpretations are possible and the current design cannot definitively address which explanation fits best. Future studies should include direct measurement of other factors that could impact performance on probabilistic classification tasks. Furthermore, probabilistic classification learning only represents one variant of implicit learning, and thus these findings may not generalize to all forms of implicit learning in healthy and BN participants. Lastly, inclusion of only women with BN make it impossible to generalize these results to men with BN or persons with other eating disorders.

Despite these limitations, these findings add to our understanding about frontostriatal deficits across development in BN, and have important implications for our understanding of BN pathophysiology. A better grasp of how and when neural processes go awry in BN, as well as how these processes contribute to the development or progression of the disorder could inform novel clinical interventions geared toward improving regulatory processes and relearning feeding/exercise habits. Likewise, identification of potential biomarkers could contribute to successful early-identification efforts or serve as indicators of treatment response. Future research should identify whether abnormal striatal-based processes are responsive to behavioral or pharmacological treatment, and if targeting deficits in both regulatory and implicit processes in treatment can improve functioning for persons with BN.

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References

- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5. American Psychiatric Association; Arlington, VA: 2013. DSM5
- Beck, A.; Steer, R.; Brown, G. Manual for the Beck Depression Inventory. Psychological Corporation; San Antonio, TX: 1996.
- Casey B, Somerville LH, Gotlib IH, Ayduk O, Franklin NT, Askren MK, et al. Behavioral and neural correlates of delay of gratification 40 years later. *Proceedings of the National Academy of Sciences*. 2011; 108:14998–15003.
- Celone KA, Thompson-Brenner H, Ross RS, Pratt EM, Stern CE. An fMRI investigation of the fronto-striatal learning system in women who exhibit eating disorder behaviors. *Neuro Image*. 2011; 56:1749–1757. [PubMed: 21419229]
- Cohen NJ, Poldrack RA, Eichenbaum H. Memory for items and memory for relations in the procedural/declarative memory framework. *Memory*. 1997; 5:131–178. [PubMed: 9156097]
- Cooper Z, Fairburn C. The eating disorder examination: A semi-structured interview for the assessment of the specific psychopathology of eating disorders. *International Journal of Eating Disorders*. 1987; 6:1–8.
- Daw ND, Shohamy D. The cognitive neuroscience of motivation and learning. *Social Cognition*. 2008; 26:593–620.
- DuPaul GJ. Parent and teacher ratings of ADHD symptoms: psychometric properties in a community-based sample. *Journal of Clinical Child and Adolescent Psychology*. 1991; 20:245–253.
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JB. Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition. Biometrics Research, New York State Psychiatric Institute; New York: 2002.
- Glimcher PW. Understanding dopamine and reinforcement learning: the dopamine reward prediction error hypothesis. *Proceedings of the National Academy of Sciences*. 2011; 108:15647–15654.
- Kataoka Y, Kalanithi PS, Grantz H, Schwartz ML, Saper C, Leckman JF, et al. Decreased number of parvalbumin and cholinergic interneurons in the striatum of individuals with Tourette syndrome. *Journal of Comparative Neurology*. 2010; 518:277–291. [PubMed: 19941350]
- Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1997; 36:980–988. [PubMed: 9204677]
- Knowlton BJ, Mangels JA, Squire LR. A neostriatal habit learning system in humans. *Science*. 1996; 273:1399–1402. [PubMed: 8703077]
- Knowlton BJ, Squire LR, Gluck MA. Probabilistic classification learning in amnesia. *Learning and Memory*. 1994; 1:106–120. [PubMed: 10467589]
- Kovacs, M. Children's Depression Inventory (CDI). Multi-Health Systems Inc; New York: 1992.
- Leckman JF, King RA, Bloch MH. Clinical features of Tourette syndrome and tic disorders. *Journal of Obsessive-Compulsive and Related Disorders*. 2014; 3:372–379.

- Marsh R. Dysfunctional frontostriatal control systems in bulimia nervosa. *Future Neurology*. 2009; 4:383–387.
- Marsh R, Alexander GM, Packard MG, Zhu H, Wingard JC, Quackenbush G, et al. Habit learning in Tourette Syndrome - A translational neuroscience approach to a developmental psychopathology. *Archives of General Psychiatry*. 2004; 61:1259–1268. [PubMed: 15583117]
- Marsh R, Horga G, Wang Z, Wang P, Klahr KW, Berner LA, et al. An fMRI study of self-regulatory control and conflict resolution in adolescents with bulimia nervosa. *American Journal of Psychiatry*. 2011; 168:1210–1220. [PubMed: 21676991]
- Marsh R, Maia TV, Peterson BS. Functional disturbances within frontostriatal circuits across multiple childhood psychopathologies. *American Journal of Psychiatry*. 2009a; 166:664–674. [PubMed: 19448188]
- Marsh R, Steinglass JE, Gerber AJ, O'Leary KG, Wang Z, Murphy D, et al. Deficient activity in the neural systems that mediate self-regulatory control in bulimia nervosa. *Archives of General Psychiatry*. 2009b; 66:51–63. [PubMed: 19124688]
- McDonald RJ, White NM. Parallel information processing in the water maze: evidence for independent memory systems involving dorsal striatum and hippocampus. *Behavioral and Neural Biology*. 1994; 61:260–270. [PubMed: 8067981]
- Mischel W, Shoda Y, Rodriguez MI. Delay of gratification in children. *Science*. 1989; 244:933–938. [PubMed: 2658056]
- Montague PR, Dayan P, Sejnowski TJ. A framework for mesencephalic dopamine systems based on predictive Hebbian learning. *The Journal of Neuroscience*. 1996; 16:1936–1947. [PubMed: 8774460]
- Morrell CH, Pearson JD, Brant LJ. Linear transformations of linear mixed-effects models. *The American Statistician*. 1997; 51:338–343.
- O'Doherty J, Dayan P, Schultz J, Deichmann R, Friston K, Dolan RJ. Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science*. 2004; 304:452–454. [PubMed: 15087550]
- Packard MG, Knowlton BJ. Learning and memory functions of the basal ganglia. *Annual Review of Neuroscience*. 2002; 25:563–593.
- Poldrack RA, Prabhakaran V, Seger CA, Gabrieli JD. Striatal activation during acquisition of a cognitive skill. *Neuropsychology*. 1999; 13:564. [PubMed: 10527065]
- Steinglass J, Walsh BT. Habit learning and anorexia nervosa: A cognitive neuroscience hypothesis. *International Journal of Eating Disorders*. 2006; 39:267–275. [PubMed: 16523472]
- Sutton, RS.; Barto, AG. *Introduction to reinforcement learning*. MIT Press; Cambridge, MA: 1998.
- Veltman D, van Balkom A, van den Heuvel O, Mataix-Cols D, Zwitter G, Cath D, et al. Common limbic and frontal-striatal disturbances in patients with obsessive compulsive disorder, panic disorder and hypochondriasis. *Psychological Medicine*. 2011; 41:2399–2410. [PubMed: 21557892]
- Wagner A, Aizenstein H, Venkatraman VK, Bischoff-Grethe A, Fudge J, May JC, et al. Altered striatal response to reward in bulimia nervosa after recovery. *International Journal of Eating Disorders*. 2010; 43:289–294. [PubMed: 19434606]
- Walsh BT. The enigmatic persistence of anorexia nervosa. *American Journal of Psychiatry*. 2013; 170:477–484. [PubMed: 23429750]
- Weschler, D. *Weschler Adult Intelligence Scale-Revised*. Psychological Corporation; New York: 1981.

Highlights

- BN participants show age-related differences on a probabilistic classification task.
- BN adolescents had unaffected early performance but less perseverance over time.
- BN adults took more trials to perform as well their healthy counterparts.
- Performance accuracy was inversely associated with BN symptom severity.
- Regulatory failures may extend to deficits in implicit processes with age in BN.

Figure 1. Effects of age and diagnosis on accuracy across blocks of the Weather Prediction Task, controlling for participant BMI, IQ, and duration of illness. Interaction of age and diagnosis is significant.

Figure 2.

Effects of age and diagnosis on latency across blocks of the Weather Prediction Task, controlling for participant BMI, IQ, and duration of illness. Main effects of age were significant, whereas main effect of diagnosis and interaction effect of age and diagnosis were insignificant.

Table 1

Demographic and clinical characteristics of the sample.

	Combined (N=107)		Adolescents (n=39)		Adults (n=68)	
	BN (n=52)	HC (n=55)	BN (n=19)	HC (n=20)	BN (n=33)	HC (n=35)
Age (in years)	19.98 (5.14) $t(105) = 0.30, p = 0.76$	20.31 (6.04)	15.79 (1.23) $t(37) = -1.41, p = 0.17$	15.15 (1.57)	22.39 (4.98) $t(66) = 0.67, p = 0.51$	23.26 (5.65)
Body Mass Index	21.99 (2.29) $t(105) = 0.16, p = 0.87$	22.06 (2.09)	21.53 (2.56) $t(37) = 0.68, p = 0.50$	22.02 (1.86)	22.26 (2.12) $t(66) = -0.33, p = 0.75$	22.09 (2.24)
WASI FSIQ	109.2 (10.2) $t(104) = 1.52, p = 0.13$	113.0 (15.1)	106.2 (10.7) $t(37) = 0.52, p = 0.61$	108.5 (16.2)	110.9 (9.6) $t(65) = 1.61, p = 0.11$	115.6 (14.0)
Duration of Illness (in years)	4.40 (4.37)	N/A	1.68 (1.50)	N/A	6.02 (4.71)	N/A
Binge Eating Episodes (past 3 mo.)	99.77 (78.91)	N/A	62.88 (61.50)	N/A	123.88 (80.68)	N/A
Vomiting Episodes (past 28 days)	40.40 (48.59)	N/A	45.53 (42.86)	N/A	37.45 (52.02)	N/A
Medication Use	34% $Z = 6.13, p < .001$	0%	30%	0%	37%	0%
Current Comorbid Depressive Disorder	30.8% $Z = 6.79, p < .001$	0%	52.6%	0%	12.1%	0%
Current Comorbid Anxiety Disorder	11.5% $Z = 3.78, p < .001$	0%	31.6%	0%	3.0%	0%
Current Depression Symptoms	17.94 (12.26) $t(96) = -8.99, p < .001$	1.59 (2.38)	18.79 (14.72) $t(30) = -4.50, p < .001$	1.00 (1.41)	17.58 (11.29) $t(64) = -7.75, p < .001$	1.91 (2.73)
Current Inattention/Hyperactivity Symptoms	14.58 (11.25) $t(91) = -5.67, p < .001$	3.87 (4.62)	14.45 (11.61) $t(28) = -3.52, p < .001$	1.95 (2.74)	14.62 (11.32) $t(61) = -4.25, p < .001$	4.94 (5.12)
History of Anorexia Nervosa	15.9% $Z = 4.46, p < .001$	0%	6.0%	0%	22.0%	0%
History of Any Lifetime Disorder	53% $Z = 6.49, p < .001$	0%	55%	0%	52%	0%
			$Z = 10.94, p < .001$		$Z = 10.34, p < .001$	

Note: BN = Bulimia Nervosa; HC = Healthy Control; WASI FSIQ = Full-scale intelligence quotient on the Wechsler Abbreviated Intelligence Scale. To determine if adults with BN who had lifetime disorders no longer met criteria as a result of ongoing pharmacotherapy, associations between current medication use with history of lifetime disorder were assessed ($phi = -0.15, p = 0.25$).