



Patients with bulimia nervosa do not show typical neurodevelopment of cognitive control under emotional influences



Michael F.W. Dreyfuss^a, Melissa L. Riegel^b, Gloria A. Pedersen^a, Alexandra O. Cohen^a,
Melanie R. Silverman^a, Jonathan P. Dyke^a, Laurel E.S. Mayer^b, B. Timothy Walsh^b, B.J. Casey^{a,c},
Allegra I. Broft^{b,*}

^a Sackler Institute for Developmental Psychobiology, Department of Psychiatry, Weill Cornell Medical College, New York, NY, USA

^b Eating Disorders Research Unit, Department of Psychiatry, Columbia University College of Physicians and Surgeons, New York, NY, USA

^c Department of Psychology, Yale University, New Haven, CT, USA

ARTICLE INFO

Keywords:

Cognition

Self-control

Task performance and analysis

Psychopathology

ABSTRACT

Bulimia nervosa (BN) emerges in the late teen years and is characterized by binge eating and related compensatory behaviors. These behaviors often co-occur with periods of negative affect suggesting an association between emotions and control over eating behavior. In the current study, we examined how cognitive control and neural processes change under emotional states of arousal in 46 participants with ($n=19$) and without ($n=27$) BN from the ages of 18–33 years. Participants performed a go/nogo task consisting of brief negative, positive and neutral emotional cues and sustained negative, positive and neutral emotional states of arousal during functional magnetic resonance imaging (fMRI). Overall task performance improved with age for healthy participants, but not for patients with BN. These age-dependent behavioral effects were paralleled by diminished recruitment of prefrontal control circuitry in patients with BN with age. Although patients with BN showed no difference in performance on the experimental manipulations of negative emotions, sustained positive emotions related to improved performance among patients with BN. Together the findings highlight a neurodevelopmental approach towards understanding markers of psychopathology and suggest that sustained positive affect may have potential therapeutic effects on maintaining behavioral control in BN.

1. Introduction

The diagnosis of bulimia nervosa (BN) – characterized by episodes of binge eating followed by compensatory behaviors, most commonly purging (APA, 2013) – emerges and peaks in late adolescence (Hudson et al., 2007). Binge eating may be conceptualized as a failure to maintain control over eating behavior following periods of restricted eating, often exhibited by patients with BN to manage their weight (Davis et al., 1988; Hay and Claudino, 2010). Binge eating and purging behaviors typically arise in the late teen years (Stice et al., 1998), a time when there is continued development in cognitive control capacity under emotional influences (Cohen et al., 2016a). This developmental period is also a time of continued development of prefrontal circuitry implicated in cognitive and emotional regulation (Gogtay et al., 2004; Silvers et al., 2016). Late adolescence and early adulthood may therefore provide a sensitive window of time for understanding the emergence and maintenance of lapses in self-control implicated in BN psychopathology.

Loss of control over eating behavior in BN often occurs in response to negative emotions. Patients with BN show greater mood fluctuations (Johnson and Larson, 1982), poorer awareness of internal emotional states (Sim and Zeman, 2004), less acceptance of their own emotions (Svaldi et al., 2012) and difficulty in mood regulation (Brockmeyer et al., 2014; Whiteside et al., 2007) relative to healthy controls (HCs). Ecological momentary assessment studies have revealed that negative affect, in particular, tends to increase prior to a binge episode (Berg et al., 2013; Haedt-Matt and Keel, 2012; Smyth et al., 2007). Negative urgency – the tendency to act more impulsively when experiencing negative emotions – in addition to the expectancy that eating will diminish negative affect have both been associated with BN (Anestis et al., 2009; Hayaki, 2009) and binge eating behaviors (Fischer et al., 2012). Binge eating may therefore represent a maladaptive coping mechanism providing temporary relief from negative affect, together with a diminished self-control capacity when trying to restrict food intake (Abraham and Beumont, 1982; Heatherton and Baumeister, 1991).

* Correspondence to: Eating Disorders Research Unit, Department of Psychiatry, Columbia University, 1051 Riverside Drive, Unit 98, New York, NY 10032, USA.
E-mail address: aib8@columbia.edu (A.I. Broft).

Cognitive control capacity has been tested in patients with BN using laboratory tasks such as the go/nogo, Stroop and stop signal tasks. These studies have produced mixed results, with a recent meta-analysis showing a small effect of decreased inhibitory control among patients relative to HCs (Wu et al., 2013). However, cognitive control tasks that include motivational cues such as food stimuli (Mobbs et al., 2008) or monetary loss (Rosval et al., 2006) consistently show diminished self-control in patients with BN. These findings suggest that loss of control in BN may be precipitated by reactivity to specific triggers and a sensitivity to rewards and punishments (Jansen, 1998), or an imbalance between reward drive and cognitive control capacity (Wierenga et al., 2014). A fundamental aspect of how individuals experience reward and punishment, especially during adolescence, is through their social interactions. Thus, patients with BN may be particularly sensitive to social cues (e.g., social and emotional facial expressions) associated with positive and negative outcomes.

In the current study, we use the psychophysiological validated Cognitive Control Under Emotions task (CCUE; Cohen, et al., 2016b) together with fMRI to examine how cognitive control and neural processes change under social and emotional influences from late adolescence into adulthood (18–33 years) in patients with BN relative to HCs. This task is a modified go/nogo task that measures the effects of brief vs. sustained negative and positive emotional states on cognitive control capacity. Prior findings from this task indicate that cognitive control, particularly under negative arousal, shows significant continued improvement from the late teen years into the mid-twenties that is paralleled by enhanced recruitment of prefrontal control circuitry (Cohen et al., 2016a). These regions show protracted maturation into young adulthood (Gogtay et al., 2004; Sowell, 2004), suggesting a relationship between development of these regions and self-control. In the current study, we chose an age range for patients and HCs that would allow us to examine this late development of cognitive control capacity under socioemotional influences and at a time when the diagnosis of BN peaks (Hudson et al., 2007; Stice et al., 1998). We hypothesized that patients with BN would show diminished cognitive control under negative arousal relative to HCs. Given the emergence of BN in late adolescence, we predicted that patients with BN would show diminished improvement in cognitive control capacity with age, particularly under negative emotions. We expected these behavioral patterns would be paralleled by functional differences in prefrontal circuitry implicated in cognitive and emotion regulation (Cohen et al., 2016a).

2. Methods

2.1. Participants

Fifty-two participants completed the study including 22 patients with BN (21 F, ages 18.4–32.8 years, $M = 25.11$, $SD = 3.98$) and 30 HCs (29 F, ages 18.4–32.1 years, $M = 23.13$, $SD = 3.38$). Each group included one age-matched (24.1 years-old) male. HCs were recruited from the community via flyers and street fairs, and screened for any personal history of psychiatric or neurologic illness at Weill Cornell Medical College. Twenty-seven of the HC participants were included in two previous studies using this paradigm (Cohen et al., 2016a, 2016b). The

Eating Disorders Research Unit of New York State Psychiatric Institute/Columbia University Medical Center recruited patients with BN, and confirmed the diagnosis by clinical interview and the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (First et al., 2002). Patients were further evaluated by the Eating Disorders Examination (Edition 16.0D; Fairburn et al., 2008) for frequency of objective bulimic episodes (OBEs) over the preceding 28 days, defined by 1) a loss of control and 2) a large amount eaten. Inclusion criteria were a duration of diagnosis > 3 months, engagement in purging via self-induced vomiting, and weight within 80–160% of ideal body weight (Metropolitan Life Insurance Company, 1959). Exclusion criteria for all participants included any significant medical or neurologic illness, other major Axis I illness, left-handedness and pregnancy. At the time of testing, 5 patients had a diagnosis of major depressive disorder. One participant on a stable dose of antidepressant medication for over 1 month prior to testing was included. Participants taking other psychotropic medications were excluded. Six patients had a history of anorexia nervosa. In addition, all patients were screened for the presence of metal in the body. Medication, body weight, comorbidities, duration of illness, history of bulimic episodes or binges over the previous 28 days were not associated with performance nor changed the significance of the findings. This study was approved by Institutional Review Boards at both sites, and all participants provided informed consent prior to participation. No data from this patient group from this experimental paradigm have previously been published.

2.2. Experimental task

Participants completed six runs of the CCUE task. This adapted emotional go/nogo task consists of brief presentations of socio-emotional cues of smiling (happy), fearful and calm (neutral) facial expressions. Participants are instructed to press to a specific target emotion (“go” trial) while withholding responses to other nontarget (“nogo”) emotions (Cohen et al., 2016b). The task consists of six runs representing each combination of emotional expression (neutral, fear, happy) as a go or a nogo stimulus. The order of runs was pseudo-counterbalanced across participants. To induce sustained states of emotional arousal, stimuli were superimposed on color backgrounds (teal, purple and yellow), and participants were informed that each color background indicated the possibility of a different outcome. Participants were instructed that an aversive noise (“negative” state) might occur at uncertain intensity and frequency, that a cash reward up to \$100 (“positive” state) could occur of uncertain value or that nothing would occur (“neutral” state; Fig. 1), and that these outcomes would not be related to task performance. The pairing of color background to the 3 different uncontrollable and unpredictable outcomes was counterbalanced across individuals. Each color background occurred twice for 75-seconds during each run of the task. In reality, each individual heard the aversive noise and won a \$20 reward exactly once during the task. The negative and positive emotional state manipulation has previously been shown to successfully induce a state of arousal relative to the neutral emotional state based on increased galvanic skin responses and self-report (Cohen et al., 2016b).

The experimental task was presented using E-prime 1.0, and

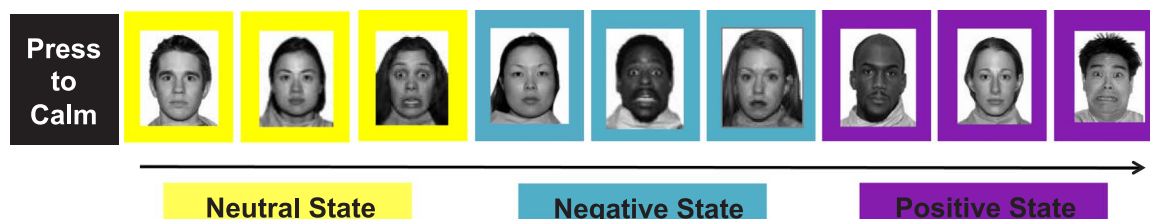


Fig. 1. Schematic of the Cognitive Control Under Emotion (CCUE) task. Participants were instructed to press to a target face emotion and withhold a response to nontarget emotions under different emotionally arousing states. Emotional states were indicated by different colored backgrounds, signaling the possibility that an aversive noise (negative state), cash reward (positive state) or no event (neutral state) would occur.

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