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The role of BIS/BAS in the vulnerability for depression in adolescent girls

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ABSTRACT

Reinforcement Sensitivity Theory (RST), the original (i.e. Gray, 1982) or revised (Gray & McNaughton, 2000), has yet to be used as a framework for investigating vulnerability to Major Depressive Disorder (MDD) in adolescents. The present study employed a high-risk design to examine whether aberrant BIS-FFFS/BAS activity was similarly present in both depressed girls and girls at high risk for depression.

Methods: $N = 85$ age-matched biological daughters of mothers with differential MDD status: (a) MDD ($n = 17$), (b) high-risk ($n = 34$), and (c) healthy controls ($n = 34$) completed measures of the BIS/BAS, depression, and anxiety.

Results: MDD girls scored significantly higher on BIS than healthy controls but not high-risk girls, and the high-risk and control groups did not differ. No group differences were found on BAS or FFFS-Fear.

Conclusions: Elevated BIS was not identified as a vulnerability factor for MDD; however, it does distinguish depressed adolescents from healthy controls.

1. Introduction

Revised *Reinforcement Sensitivity Theory* (RST; Gray & McNaughton, 2000) posits that three neurobiological systems govern sensitivity to reinforcement: the behavioral approach system (BAS), the fight–flight–freeze system (FFFS), and the behavioral inhibition system (BIS). The BAS underlies sensitivity to reward and guides approach behavior and motivation for appetitive stimuli, with relations to positive emotions such as joy, elation, hope, and relief (e.g. avoidance of punishment). The FFFS drives avoidant behavior from aversive stimuli, both unconditioned and conditioned, and is associated with fear. Lastly, the BIS is activated during conflict between the BAS and the FFFS such that ongoing approach behavior is inhibited when threat is detected, thereby delaying approach and promoting withdrawal; it is intrinsically linked to anxiety and associated with negative affect. The original (i.e. Gray, 1982) and revised (Gray & McNaughton, 2000) versions of RST operated under the assumption that BIS/FFFS and BAS have independent and separable effects; however, Corr's (2002) *joint subsystems hypothesis* posits that these systems have both antagonistic and facilitatory effects on one another and thus act interdependently in guiding approach–avoidance behavior.

Over recent decades, RST (original and revised) has been applied to study a range of psychopathology. A major focus has been Major Depressive Disorder (MDD), a debilitating mental illness marked by primary features of depressed mood and/or loss of interest or pleasure. MDD can be characterized by reduced approach behavior, through motivational deficits and/or a lack of positive reinforcement, and increased avoidance behavior (e.g. social withdrawal). Indeed, studies with adult clinical populations, using the original RST framework, have revealed depression to be associated with low BAS and high BIS. Kasch, Rottenberg, Arnow, and Gotlib (2002) found MDD patients to exhibit lower BAS and higher BIS than their healthy counterparts, and levels of BIS/BAS were stable over an 8-month period. Furthermore, results suggest that low BAS is more integral to depression and may serve as a unique vulnerability, as only BAS was significantly correlated with depression severity. Concordantly, low BAS has been found to predict depressive onset, average weekly level of depression, number of symptoms at follow-up, and time to recovery (McFarland, Shankman, Tenke, Bruder, & Klein, 2006). Pinto-Meza et al. (2006) provided further support for the unique and stable role of BAS by finding that low BAS was similarly present in individuals with current and remitted MDD. In contrast, BIS was only elevated in those with current depression, suggesting it may be more of a state-like feature. Of note, these studies employed original RST (i.e. Gray, 1982), which excludes the FFFS (its function being attributed to the BIS). Thus, although these findings are informative, they excluded major theoretical revisions to RST (e.g. the inclusion of FFFS, and the notion of separate vs. joint subsystems) and we are unaware of any MDD study that has applied revised RST.

The downward extension of RST to youth is important because an estimated 4–6% of adolescents currently experience MDD

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(Kessler, Avenevoli, & Merikangas, 2001), and adolescent depression is associated with significant physical, emotional, and behavioral impairment in a range of contexts (i.e. family, school, and social) (Goodyer & Sharp, 2005). Therefore, early intervention and treatment is imperative. Focusing on depression in adolescent girls is warranted as they more often become depressed, and it is during adolescence when the 2:1 female to male ratio found in depression begins to emerge (Rudolph, 2009).

To the best of our knowledge, there has yet to be an investigation of RST (original or revised) in youth with clinically-defined MDD. However, cross-sectional community studies examining symptoms of depression and anxiety in the context of original RST collectively point to significant positive associations between BIS and depression and anxiety, whereas BAS shows only weak, non-significant associations (i.e. Muris, Meesters, de Kanter, & Timmerman, 2005). In addition to these community studies, we are aware of only one investigation that employed revised RST and this was carried out with clinically-anxious outpatient adolescents (Vervoort et al., 2010). This study also tested the *joint subsystems hypothesis* (JSH) which suggests that, in the context of adolescent emotional problems, one system may dominate the other thus suppressing its effect on approach–avoidance behavior (Corr, 2002). The authors found that anxiety-disordered adolescents reported significantly higher BIS and FFFS, but not BAS, than healthy controls. Regarding their JSH analyses, BIS (which included FFFS) and BAS scores were differentially predictive of anxiety symptoms between groups such that in healthy controls both BIS and BAS were predictive of anxiety, while in the anxious group only BIS was predictive. These results provided support for the JSH and consistent with Corr (2002), suggest that differential antagonistic/facilitatory effects may be indicative of psychopathology.

While the study of revised RST and the JSH in clinically-defined adolescent MDD is in itself worthwhile, an additional important consideration is whether these neurobiological systems and their interactive effects constitute vulnerability factors for depression. Adult findings, using original RST, suggest that low BAS serves as a trait-vulnerability for depression while high BIS is a state-like feature (Pinto-Meza et al., 2006). However, these studies were correlational and it is uncertain whether low BAS serves as a vulnerability to depression in general (e.g. across the lifespan). By investigating individuals before their first episode, using high-risk or longitudinal designs, true vulnerability factors for MDD can be examined (Gotlib et al., 2010), and we are unaware of either such investigations of RST (original or revised) in adolescent MDD.

As such, this is the first investigation of the utility of RST in identifying adolescents with MDD. By employing a high-risk design, our primary aim was to investigate whether BIS-FFFS/BAS serves as a vulnerability factor for depression. The underlying idea was that if high-risk girls reported a similar BIS-FFFS/BAS profile as depressed girls, in relation to healthy controls, findings would provide support for BIS-FFFS/BAS as a vulnerability factor. Girls were matched on age to control for its effect on level of depression (Angold, Erkanli, Silberg, Eaves, & Costello, 2002), and we controlled for anxiety given high rates of comorbidity (Kessler et al., 2001). We hypothesized that elevated BIS/FFFS would be a vulnerability factor for MDD and, given the lack of relation between depressive symptoms and BAS in youth, we expected no group differences on BAS. A subsidiary aim was to test the JSH as it relates to depressive symptoms, and examine whether differential BIS-FFFS/BAS function would also serve as a vulnerability factor. Given the findings by Vervoort et al. (2010), we expected that both BIS and BAS would be predictive of dimensional scores of depression in healthy controls, while only BIS would be predictive in the high-risk and MDD groups. Thus, this differential function would also serve as a vulnerability factor for depression. Lastly, given debates around categorical vs. dimensional approaches to conceptualizing depression in adolescents (Hankin, Fraley, Lahey, & Waldman, 2005), our final aim was to examine relations between BIS and depression dimensionally (regardless of group status). Since the empirical literature suggests that BIS is intrinsically linked to anxiety (Muris, Merckelbach, Schmidt, Gadet, & Bogie, 2001), and given the high comorbidity between anxiety and depression in youth (Kessler et al., 2001), we included anxiety as a potential confounding variable.

2. Method

2.1. Participants

$N = 85$ girls aged 10–16 ($M = 12.87$, SD = 1.99) comprised three age-matched groups who differed in their risk status: (1) currently depressed biological offspring of mothers with a history of MDD (MDD: $n = 17$); (2) never-depressed biological offspring of mothers with a history of depression (high-risk: $n = 34$); (3) never-depressed biological offspring of mothers with no history of depression (healthy controls: $n = 34$). Comorbidity within the MDD group included separation anxiety disorder ($n = 5$), post-traumatic stress disorder ($n = 2$), obsessive–compulsive disorder ($n = 3$), panic disorder ($n = 2$), social phobia ($n = 2$), agoraphobia ($n = 2$), and specific phobia ($n = 3$).

Inclusion criteria required girls to be between 10 and 16 years-old, fluent in English, possess adequate academic skills as determined by the Wide Range Achievement Test 4 (WRAT4; Wilkinson & Robertson, 2006), meet appropriate psychiatric criteria for group assignment, and have a living mother that was also eligible. If participants failed to meet full criteria, had a psychotic disorder or any learning disability or mental retardation, they were excluded. Participants responded to community advertisements and were recruited from local inpatient and outpatient clinics for adolescents.

2.2. Measures

2.2.1. Structured clinical interview for DSM-IV TR Axis I disorders

The SCID-I (First, Spitzer, Gibbon, & Williams, 2002) was conducted to determine MDD status in mothers. For the assessment of MDD and comorbid psychiatric disorders, all modules were used. Moderate to excellent inter-rater reliability has been found for the SCID-I (mean kappa = 0.71; Lobbestael, Leurgans, & Arntz; 2011).

2.2.2. NIMH diagnostic interview schedule for children – Version IV

To determine MDD status in girls, the NIMH DISC-IV (Shaffer, Fisher, Lucas, Dulcan, & Schwab Stone, 2000) was conducted. The DISC-IV is a highly structured and comprehensively designed interview to assess psychiatric disorders in children and adolescents. All interviews were conducted by doctoral graduate students and clinical research assistants whom had completed training under the supervision of the principal investigator.

2.2.3. BIS/BAS scales

The BIS/BAS scales (Carver & White, 1994) is a self-report measure consisting of 20 questions, rated *Very True* = 1 to *Very False* = 4, that traditionally comprise 4 separate scales: BIS, BAS-Drive (goal-directed motivation), BAS-Reward Responsiveness (response upon receipt of reward), and BAS-Fun Seeking (desire for novel rewards). Consistent with revised RST, we formed two scales from the BIS items: BIS and FFFS-Fear (Heym, Ferguson, & Lawrence, 2008). Maximum scores for the scales are as follows: BIS, 16; FFFS-Fear, 12; BAS-Drive, 16; BAS-Reward Responsiveness, 20; and BAS-Fun

Seeking, 16. For regression analyses, a BAS total score was used which is the sum of the individual BAS scales. Convergent and discriminant validity for the BIS/BAS scales has been supported (Jorm et al., 1999). In the current study, internal consistency, as measured by Chronbach's α, was 0.70 for BIS, 0.12 for FFFS-Fear, and 0.79 and for the BAS higher-order dimension, respectively. Aside from the low internal consistency of FFFS-Fear, for a measure of this length these reliabilities are adequate (Slobodskaya, 2007).

2.2.4. The mood and feelings questionnaire

The MFQ (Angold, Costello, Pickles, & Winder, 1987), a 33-item self-report measure for children and adolescents, was used to assess adolescent depressive symptoms over the prior two-week period (maximum score = 66). In the current study, the MFQ had an α of 0.94.

2.2.5. The multidimensional anxiety scale for children

The MASC (March, 1997) is a developmentally appropriate 39-item self-report measure of anxiety for youth (maximum score = 117). In the current study, the MASC had an α of 0.93.

2.2.6. Procedures

This study was approved by the appropriate institutional review board. Those interested in the study were required to complete phone screens, and if eligible, were invited to participate. Mothers and daughters completed structured clinical interviews to determine group assignment. For daughters, MDD group membership required a diagnosis of depression; high-risk group membership required no diagnosis of current or past depression; and healthy controls were required to be free from psychiatric disorder (current or lifetime). For mothers, MDD and high-risk group membership required a lifetime diagnosis or recurrent MDD since their daughter's birth, and healthy controls were free from psychiatric disorder (current or lifetime). Mothers and daughters completed structured clinical interviews separately, and daughters completed self-report measures in private.

3. Results

3.1. Participant characteristics

For participant characteristics, please see Table 1. Groups were compared on socio-demographic characteristics and there were no significant differences for age, race, family annual income, or WRAT scores. One-way ANOVAs revealed significant differences between groups on symptoms of depression and anxiety. On the MFQ, $F(2, 82) = 28.402$, $p < .001$, $\eta^2 = 0.409$, MDD girls differed from the high-risk ($p < .001$) and control girls ($p < .001$), with the high-risk group also scoring higher than controls ($p = 0.039$). Similarly on the MASC, $F(2, 82) = 9.974$, $p < .001$, $\eta^2 = 0.196$, the MDD girls differed from the high-risk ($p < .001$) and control groups ($p < .001$); however, the high-risk girls did not differ from controls ($p = 0.781$).

3.2. Bivariate correlations

Significant positive correlations were found between the MFQ and BIS ($r = 0.421$; $p < .001$), MFQ and FFFS-Fear ($r = 0.236$; $p = 0.030$), MASC and BIS ($r = 0.470$; $p < .001$), MASC and FFFS-Fear ($r = 0.290$; $p = 0.007$), and MFQ and MASC scores ($r = 0.684$; $p < .001$). The BIS/BAS scales correlated with each other as expected (see Carver & White, 1994). BAS-Reward Responsiveness significantly correlated with BAS-Drive ($r = 0.469$; $p < .001$), BAS-Fun Seeking ($r = 0.452$; $p < .001$), and BIS ($r = 0.311$; $p = 0.004$). BAS-Drive significantly correlated with FFFS-Fear ($r = -0.248$; $p = 0.022$) and BAS-Fun Seeking ($r = 0.571$; $p < .001$). BAS-Fun Seeking also significantly correlated with FFFS-Fear ($r = -0.217$; $p = 0.046$).

3.3. Group differences on the BIS/BAS scales

ANOVA results demonstrated a significant difference between groups on the BIS scale, $F(2, 82) = 5.524$, $p = 0.006$, $\eta^2 = 0.119$, with the MDD group scoring higher than healthy controls ($p = 0.004$). However, the difference between the MDD and high-risk groups was not significant ($p = 0.070$); the high-risk and control groups did not differ either ($p = 0.385$). There were no significant differences on FFFS-Fear and BAS scales: FFFS-Fear, $F(2, 82) = 1.020$, $p = 0.365$, $\eta^2 = 0.024$, BAS-Drive, $F(2, 82) = 0.561$, $p = 0.573$, $\eta^2 = 0.014$, BAS-Reward Responsiveness, $F(2, 82) = 2.180$, $p = 0.120$, $\eta^2 = 0.050$, and BAS-Fun Seeking, $F(2, 82) = 0.504$, $p = 0.606$, $\eta^2 = 0.012$ (see Table 2).

Lastly, an ANCOVA was conducted to determine if group differences on BIS would remain after controlling for anxiety and results were non-significant, $F(2, 81) = 1.472$, $p = 0.235$, $\eta^2 = 0.035$. There was a strong relationship between anxiety and BIS (partial $\eta^2 = 0.147$).

Table 1
Participant characteristics.

	MDD ($n = 17$)	High-risk ($n = 34$)	Healthy control ($n = 34$)	p[a]
Daughter age	13.06 (1.89)	12.88 (1.98)	12.76 (2.10)	0.885
Mother age	42.00 (7.98)	39.91 (6.40)	40.33 (6.80)	0.316
Family yearly income	41.30 K (24.80 K)	50.70 K (30.70 K)	63.70 K (39.60 K)	0.241
Daughter MFQ	27.35 (12.41)	12.94 (9.90)	7.59 (4.72)	<.001
Daughter MASC	61.94 (20.42)	41.34 (20.67)	38.33 (14.75)	<.001
Maternal MDD episodes	4.27 (2.28)	3.68 (3.08)	N/A	0.562
Maternal age 1st episode	21.20 (11.30)	29.00 (8.99)	N/A	0.044
WRAT	99.60 (9.23)	104.90 (14.86)	107.35 (18.57)	0.290
Race				
Black	5	5	8	$\chi^2 = 2.833$; $p = 0.933$
White	4	4	6	
Hispanic	6	12	11	
Asian	0	1	0	
Family history of MDD beyond maternal MDD	6	9	8	$\chi^2 = 4.623$; $p = 0.598$

Note: Data are mean (standard deviation). MFQ = Mood and Feelings Questionnaire (depressive symptoms of daughters); MASC = Multidimensional Anxiety Scale for Children; WRAT = Wide Range Achievement Test 4. Some participants chose not to identify race accounting for the fact that group sizes do not add up to the full sample size.
[a] p-Value of One-Way ANOVA, otherwise noted as Chi-Square test.

Table 2
Descriptive statistics and group differences on the BIS/BAS scales.

	MDD (n = 17)	High-risk (n = 34)	Healthy control (n = 34)	p[a]	η^2	Group difference
BAS-D	10.88 (2.60)	10.94 (2.57)	10.28 (2.89)	0.573	0.014	
BAS-RR	17.12 (1.96)	17.80 (1.69)	16.76 (2.43)	0.120	0.050	
BAS-F	12.63 (2.13)	11.96 (2.29)	12.13 (2.27)	0.606	0.012	
BIS	13.47 (2.29)	11.76 (2.86)	10.94 (2.36)	0.006	0.119	MDD > HC
FFFS-Fear	8.44 (2.36)	7.85 (1.56)	7.71 (1.61)	0.365	0.024	

Note: Data are mean (standard deviation). BAS-D = BAS-Drive; BAS-RR = BAS-Reward Responsiveness; BAS-F = BAS-Fun Seeking; BIS = Behavioral Inhibition System; FFFS-Fear = Fight-flight-freeze System.
[a] p-Value of the one-way ANOVA.

3.4. Testing the JSH in relation to depressive symptoms

Following Vervoort et al.'s (2010) approach to testing the joint subsystems hypothesis, we examined whether there were differential relations between BIS-FFFS/BAS and MFQ scores between groups. Due to low statistical power, the high-risk and MDD groups were combined. Thus, two separate linear regressions were performed, one for healthy controls and another for high-risk/MDD girls, with BIS (FFFS included) and BAS (total score) entered as predictor variables and MFQ scores as the outcome variable. In the healthy control group, neither BIS ($\beta = 0.019$; SE = 0.297; $t = 0.063$, $p = 0.950$) nor BAS ($\beta = 0.050$; SE = 0.139; $t = 0.357$, $p = 0.723$) was predictive of MFQ scores. In the high-risk/MDD group, BIS was a significant predictor ($\beta = 1.372$; SE = 0.411; $t = 3.343$, $p = 0.002$) but BAS was not ($\beta = -0.152$; SE = 0.307; $t = -0.494$, $p = 0.623$). Multicollinearity among predictors was not present in these analyses (Tolerance $\leqslant$ 0.998, VIF $\leqslant$ 1.068).

3.5. Regression analysis to assess dimensional associations between depression and BIS

Linear regression was performed to determine whether dimensional scores of depression predicted BIS, across groups, after controlling for anxiety. These analyses were not conducted for BAS or FFFS-Fear since groups did not differ. MFQ and MASC scores were entered as predictors, with BIS as the outcome. The model explained 23.9% of the total variance in BIS, $R^2 = 0.239$, $F(2, 82) = 12.882$, $p < .001$, and anxiety was the only significant predictor ($\beta = 0.342$; SE = 0.018; $t = 2.588$, $p = 0.011$), depression was non-significant ($\beta = 0.187$; SE = 0.031; $t = 1.415$ $p = 0.161$). There was no multicollinearity among predictor variables (Tolerance = 0.532, VIF = 1.879).

4. Discussion

The current study was the first to utilize a high-risk design to examine RST (original or revised) in the context of clinically-defined MDD in youth. Contrary to our primary hypothesis, we found no evidence of BIS-FFFS/BAS serving as a vulnerability factor for depression. Although the MDD and high-risk groups exhibited similar BIS, the high-risk group did not differ from controls and there were no group differences on FFFS. Consistent with hypotheses, no group differences were found in terms of BAS. These results generally support prior findings that high BIS is likely a correlate (or consequence) of current depressive episodes rather than a cause (Pinto-Meza et al., 2006). While we found that high-risk girls evidenced significantly higher levels of depression than controls, higher levels of depression were not accompanied by elevated BIS suggesting that BIS operates differently in the context of clinical depression. However, given the likely heterogeneity in the degree of vulnerability to depression in girls in the high-risk group, we cannot make this conclusion with certainty. It is likely that some of the high-risk girls exhibited BIS that was more similar to the MDD group, while others were more similar to healthy controls.

In providing a preliminary BIS-FFFS/BAS profile for depressed adolescents, we found adolescent MDD to be characterized by elevated BIS. In the context of original RST, these results are consistent with youth community-based studies (i.e. Jorm et al., 1999) but differ from adult findings that hypoactive BAS is the dominant system in depression (Kasch et al., 2002). Given that elevated BIS is associated with negative affect, it has been suggested that depressed mood may be more integral to depression than anhedonia (Lewinsohn, Petit, Joiner, & Seeley, 2003). Gray (1991) posited that BAS activity in anhedonic depression and mixed anxiety-depression would differ, and in teasing apart BIS and BAS within these depressive subtypes, low BAS has been found to be solely predictive of anhedonic depression suggesting that high BIS appears to be more integral to depression and anxiety (Kimbrell, Nelson-Gray, & Mitchell, 2007). Developmentally, aversive motivation may substantially disrupt appetitive motivation such that frustrative non-reward is first met with a strong aversive response which over time becomes extinct, leaving a sense of hopelessness about the future and reduced approach behavior (Fowles, 1988). In the present study, we did not measure anhedonia specifically; however, we would argue that lower scores on the BAS scales could serve as a proxy for anhedonic symptoms, and MDD girls scored equally as high as the other groups. Thus, it may be a possibility that comorbid anxiety, more strongly associated with BIS, in the MDD group may have played a role in our findings. Another explanation may stem from the fact that the BAS is continuously developing through adolescence (Galván, 2013) and low BAS scores may only represent a characteristic of and vulnerability factor for depression in adulthood, after reward and underlying neural systems have fully matured.

Regarding the JSH, our findings suggest that BIS may be the dominant system in adolescent depression, but we are unable to make any definitive conclusions regarding separate vs. joint effects. In healthy controls, neither BIS (FFFS included) nor BAS were predictive of depressive symptoms, which conflicts with Corr's (2002) prediction that both systems should be significant predictors. Despite that some evidence was provided for the JSH, as BIS was the only significant predictor of depressive symptoms for the high-risk/MDD combined group, the relative contributions of the scores of high-risk vs. MDD girls is unclear.

For our last aim, regression analyses revealed that depression was a non-significant predictor of BIS after controlling for anxiety. This finding supports the notions that anxiety, rather than depression, is most strongly associated with behavioral inhibition and, though mediation was not conducted, that anxiety accounts for the BIS-depression relationship (Muris et al., 2001).

This study offers novel findings, but it is not without limitations. A small MDD sample size, cross-sectional data, and a reliance

on self-report measures are of note. Conclusions drawn from our findings with the JSH are limited as we lacked the statistical power to truly test whether dominance of the BIS is present in adolescent MDD, and also whether this serves a vulnerability factor. Regarding FFFS-Fear, the scale had particularly low internal consistency which makes our finding of no group differences questionable. This study would have benefitted from a pubertal measure given the developmental effects of puberty on motivational systems, and its role in moderating the relation between psychophysiology and behavioral measures (Quevedo, Benning, Gunnar, & Dahl, 2009). Despite these limitations, this is the first study to provide a BIS-FFFS/BAS profile for depressed adolescents, and the first to examine BIS-FFFS/BAS as a vulnerability factor for adolescent MDD. In addition, rigorous effort went into group assignment, aided by structured clinical interviews and strict exclusion criteria.

Although these findings are preliminary in nature, this investigation notably extends the application of RST to MDD by studying vulnerability to depression in adolescents and by employing recent RST theory (revised RST and the JSH). Future research examining vulnerability to depression should continue to employ these recent iterations of RST, and a focus on mid- to late-adolescent depression is warranted as BAS, rather than BIS, may be the dominant system.

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