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Bias to negative emotions: A depression state-dependent marker in adolescent major depressive disorder

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ABSTRACT

The aim of the current research was to examine for the first time the extent to which bias to negative emotions in an inhibitory control paradigm is a state or trait marker in major depressive disorder (MDD) in adolescents. We administered the affective go/no go task which measures the ability to switch attention to or away from positive or negative emotional stimuli to 40 adolescents with MDD (20 in acute episode (MDDa) and 20 in remission (MDDr)) and 17 healthy controls (HC). MDDa were significantly faster on the shift to negative target blocks as compared to shift to positive target blocks while HC and MDDr displayed the opposite pattern as measured by an "emotional bias index" (EBI = latency (shift to negative targets) − latency (shift to positive targets)). There was also a trend for an effect of group on commission errors, suggesting more impulsive responding by MDDa than both MDDr and HC independently of stimulus valence throughout the task. Negative bias was not associated with depression severity or medication status. In conclusion, bias to negative emotional stimuli appears to be present in the acute stage of MDD and absent in remission suggesting that it is a depression state-specific marker of MDD in adolescents. Latency emerges as a better proxy of negative bias than commission errors and accuracy on this inhibitory control task in adolescents with MDD.

1. Introduction

Major depressive disorder (MDD) is a prevalent and recurrent condition in children and adolescents, and it is associated with substantial impairment as seen in difficulties in school, interpersonal relationships, tobacco and substance abuse, suicide attempts, and a 30-fold increased risk of completed suicide (Lewinsohn et al., 1998). There is strong evidence that MDD is associated with impaired emotion regulation, of which voluntary and involuntary (automatic) cognitive processes are key components (Mayberg, 2007; Phillips et al., 2008).

Inhibitory control, which includes selective attention (i.e. to direct or redirect attention toward goal-related stimuli), and inhibition (i.e. to distract from goal-irrelevant stimuli) play significant roles in voluntary emotion regulation and are impaired in mood disorders, particularly in depression. Inhibitory control is involved in modulating the effect of emotional stimuli on behavior by redirecting attention to goal-oriented information and inhibiting irrelevant information. These strategies are at the core of emotion regulation in MDD (Joormann and Gotlib, 2010). The go/no go paradigm has been traditionally used as a measure of inhibitory control. The addition of an affective component to this paradigm makes it relevant to mood disorders (Murphy et al., 1999; Ladouceur et al., 2005). The affective go/no go task specifically measures bias to emotional stimuli in an inhibitory control paradigm, a paradigm that is clinically relevant when working with depressed patients.

Numerous studies have used the affective go/no go paradigm as a measure of bias to emotional stimuli in depressed adults and adolescents through contrasting reaction times for happy stimuli to reaction times for sad stimuli (Murphy et al., 1999; Erickson et al., 2005; Kyte et al., 2005; Kaplan et al., 2006; Rubinsztein et al., 2006). For example, depressed adults have been found to respond more rapidly to sad than happy word targets and omit more happy word targets than sad targets on this task (Murphy et al., 1999; Erickson et al., 2005), a negative bias that was independent of medication status (Erickson et al., 2005). In addition, acutely depressed and

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remitted adolescents, when studied as one group, showed a bias towards negatively valenced word stimuli as they were more accurate in their responses to sad targets than controls (Kyte et al., 2005).

In the present study we aimed to use the affective go/no go task to determine the extent to which bias to negative emotional stimuli was present in adolescent MDD, and whether it was only present when subjects were asked to shift attention to a new emotional valence (i.e. when inhibitory control is mostly needed). Discriminating between state and trait markers of MDD may be the first step to help identify markers of response and/or guide choice of interventions (Mayberg et al., 1997; Gorlyn et al., 2008), in addition to identifying vulnerability for the illness. State markers, present only during the acute episodes of MDD, are more likely to help predict treatment response and guide treatment choice (Mayberg et al., 1997; Gorlyn et al., 2008). On the other hand, trait markers may represent vulnerability to, or lasting effect of the illness. Previous studies in pediatric MDD were not specifically designed to examine whether bias to negative emotions was a state or trait marker of the illness; to do so in this study, we included adolescent participants with MDD in acute and remitted states in separate groups and studied three groups of participants: acutely depressed (MDDa), remitted (MDDr) and healthy controls (HC). We hypothesized that MDDa would show a bias towards negative stimuli (i.e. they would be slower in responding to positive stimuli as compared to negative stimuli). Existing findings did not allow us to hypothesize whether this bias would only be present when subjects were asked to shift attention to a new emotional valence or whether it would be observed throughout the task. We also hypothesized that this impairment would not be observed in MDDr and HC.

2. Methods

2.1. Participants and measures

The study protocol was approved by the University of Pittsburgh Institutional Review Board. Fifty-seven adolescents in total were recruited; these included 40 participants meeting criteria for major depressive disorder (MDD), current or past, according to Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) diagnosed using the Kiddie Schedule for Affective Disorders Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997) and 17 healthy control participants (HC) with no previous psychiatric history or psychiatric history in either biological parent. Out of the 40 participants with MDD, 20 were in an acute depressive episode (MDDa), defined by a Children Depression Rating Scale (CDRS) (Poznanski et al., 1984) score ≥ 40; and 20 were in remission (MDDr), defined by a CDRS ≤ 28 at the time of testing, a commonly used remission criterion for pediatric depression (Emslie et al., 2002). The groups were balanced for age, gender-ratio, pubertal development and IQ (Table 1). A full prorated Intelligence Quotient (IQ) score was obtained through two verbal and performance subscales (vocabulary and matrix respectively) of the Wechsler Intelligence Scale for Children—IV (WISC-IV). Participants also completed the Petersen Puberty Development Scale (PDS) (Petersen et al., 1988). Exclusion criteria included a history of head injury, neurological disorder (epilepsy, developmental disorder, loss of consciousness for more than 10 min), premorbid IQ estimate <80, current psychotic symptoms, current history of alcohol and illicit substance abuse or dependence, and current or past history of attention deficit hyperactivity disorder (ADHD). All participants and their parents were made aware of the purpose of the study and signed informed consent to participate.

2.2. Affective go/no go task

The affective go/no go task involves the rapid presentation of a series of words in the center of a computer screen. Each word is displayed for 300 ms, and there is a 900-ms interval between the words. These words have a "happy/positive" or "sad/negative" valence. Participants are given a target valence and are asked to push the button on a press pad when they see a word that matches this valence, with the other valence acting as a distracter. There are 10 blocks of 18 stimuli each, with nine positive words (e.g., joyful, warmth) and nine negative words (e.g., mistake, burden) for a total of 45 negative and 45 positive words, presented randomly (Murphy et al., 1999). These are arranged in sequences of either happy or sad target valences as follows: happy–happy–sad–sad–happy–happy–sad–sad etc.… The first two blocks are considered practice blocks. These are followed by "four" shift conditions, where participants are required to inhibit responding to the previous target, and four non-shift conditions in which participants continue to respond to the same target valence as the previous block. Participants were informed of the shift as they were to begin a set-shift block. There are three dependent measures of interest: i) correct response latency or Response Time (RT), ii) total commission errors (responses to a distracter valence) and iii) total omission errors (non-responses to the target valence). For each commission error, a 500-ms/450-Hz tone sounds; participants do not get any feedback after an omission.

Omission errors on this task may indicate a difficulty disengaging from the emotion at hand. For instance, if participants commit more omission errors on happy trials, it may mean that they are experiencing difficulty inhibiting the sad affect and attending to the positive stimulus (Erickson et al., 2005). While response accuracy may be a better gauge of automatic biases, response latency may be tapping into voluntary processes of emotion regulation (Lawson and MacLeod, 1999; Sears et al., 2011), which are the main focus of the current study. Commission errors, on the other hand, indicate impulsivity in responding. These are usually more relevant to manic states and are more automatic in nature (Fleck et al., 2011).

Table 1
Demographic and clinical data.

	HC $N=17$	MDDr $N=20$	MDDa $N=20$	Statistics
Age mean (S.D.)	15.2 (1.8)	15.4 (1.3)	15.3 (1.6)	$F(2,56)=0.095$, $p=0.910$
Female:male	9:8	15:5	17:3	Chi-square $(1,57)=4.82$, $p=0.090$
IQ mean (S.D.)	112 (11)	113 (12)	105 (11)	$F(2,56)=2.938$, $p=0.061$
PDS mean (S.D.)	2.7 (0.8)	2.8 (0.5)	2.7 (0.4)	$F(2,56)=0.311$, $p=0.734$
CDRS mean (S.D.)	19.1 (2.3)	23.7 (3.4)	58.5 (10.9)	$F(2,56)=189$, $p=0.00$ HC vs. MDDr, $p=0.139$ HC vs. MDDa, $p=0.00$ MDD vs. MDDr, $p=0.00$
Total MDD episode duration mean (S.D.)[a]		1.6 (1.8)	2.1 (1.8)	$T(37)=-0.789$, $p=0.435$
Total number of MDD episodes mean (S.D.)		1.2 (0.5)	1.4 (0.6)	$T(37)=-1.366$, d.f. $=37$, $p=0.180$
Age of illness onset mean (S.D.)[a]		13.3 (2.0)	11.7 (3.0)	$T(37)=1.989$, $p=0.054$
Age of onset of current MDD mean (S.D.)[a]			13.6 (1.61)	
Age of offset of past MDD mean (S.D.)[a]		15 (1.4)		
Presence of lifetime anxiety disorders *N* (% Yes)		10 (50%)	15 (75%)	Chi-square $(1, 57)=2.67$, $p=0.102$
Receiving SSRI/SNRI *N* (% Yes)		13 (68%)	13 (68%)	Chi-square $(1,57)=0$, $p=1.0$

[a] In years.