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Compounded Deficits: The Association Between Neuropsychological Impairment and Attention Biases in Currently Depressed, Formerly Depressed, and Never Depressed Individuals

Kean J. Hsu[1,2] and Gerald C. Davison[3]
[1]Departments of Psychology and Psychiatry and Biobehavioral Sciences, University of California, Los Angeles;
[2]Behavioral Health Partial Program, McLean Hospital; and [3]Department of Psychology, University of Southern California

Abstract
Attentional dysfunction is commonly found in depressed individuals in the form of impairment on measures of selective attention as well as attentional biases for negative information. Although a relationship between nonvalenced and valenced aspects of attention has been suggested based on theory, functional neuroanatomy, and studies in other populations, this relationship has not been explicitly explored in depressed individuals. A total of 91 individuals who were currently depressed, formerly depressed, or never depressed completed tasks assessing neuropsychological functioning and attentional bias. Depression status was associated with decreased selective attention (but not set shifting) and stronger attention biases. Selective attention was also found to mediate the relationship between group status and attentional bias, but only in currently depressed individuals. These findings suggest depression is associated with specific impairments in attention and moreover that impairments in nonvalenced aspects of attention are associated with attentional bias to valenced stimuli in currently depressed individuals.

Keywords
depression, attentional bias, selective attention, neuropsychological functioning

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Major depression (MD) is a complex mental disorder with heterogeneous symptom expression. Although depressed mood and anhedonia are integral to the disorder, attention is one of the domains of functioning most consistently impacted in MD. In fact, deficits in attention are found not only in currently depressed individuals relative to healthy control groups, but also in formerly depressed (i.e., currently euthymic) individuals (Rock, Roiser, Riedel, & Blackwell, 2014), even 10 years after initial follow-up (e.g., Ardal & Hammar, 2011).

These impairments may be a stable, irreversible, trait-like marker for MD, discernible even when patients previously diagnosed with MD are in full remission. Indeed, a number of twin and familial risk studies of MD suggest that deficits in attention may be a vulnerability marker for depression (e.g., Belleau, Phillips, Birmaher, Axelson, & Ladouceur, 2013; Hsu, Young-Wolff, Kendler, Halberstadt, & Prescott, 2014). In addition, although attention, memory, and executive function are interrelated cognitive processes (Lezak, Howieson, & Loring, 2004) and processes other than attention have been, at times, found to be impaired in depression (e.g., Lampe, Sitskoorn, & Heeren, 2004), the attentional dysfunction found in MD particularly impairs other cognitive capabilities (Mialet, Pope, & Yurgelun-Todd, 1996). Deficits in attention have also been found to be significantly associated with inability to return to work, suggesting that these neuropsychological deficits have a meaningful impact on daily activity and

Corresponding Author:
Kean J. Hsu, Anxiety and Depression Research Center, Department of Psychology, University of California, Los Angeles, 1285 Franz Hall, Box 951563, Los Angeles, CA 90095-1563
E-mail: keanjhsu@ucla.edu

functioning in depressed individuals as well (a significant portion of the $210 billion economic burden of depression; Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015; McIntyre et al., 2013). Moreover, attentional impairment is associated with poorer treatment response, to both antidepressant medication (Kampf-Sherf, 2004) and cognitive-behavioral therapy (Crews & Harrison, 1995). Dysfunction in the attention system is clearly associated with MD, with a multitude of negative consequences manifesting across different domains.

One mechanism by which attention may potentially influence MD is through emotion regulation (Joormann & Quinn, 2014). Theoretical models and research from the fields of developmental psychology and affective science have implicated the role of attention in emotion regulation. Development and refinement of the executive attention system in infants and children facilitates regulation of temperamental distress (Bell & Calkins, 2012). In addition, the circuitry for the emotion-regulation system (e.g., the amygdala, anterior cingulate cortex, and prefrontal cortex) overlaps considerably with the selective attention system (Keilp, Gorlyn, Oquendo, Burke, & Mann, 2008), suggesting that dysfunction in either system could be propagated to the other. Studies experimentally manipulating attention (e.g., via nonvalenced attention training, though not necessarily targeting attention alone) have found improved emotion regulation in active manipulation groups relative to controls (Gyurak, Ayduk, & Gross, 2010; Siegle et al., 2014). Given consistent findings of nonvalenced attentional impairments in depressed individuals, it is conceivable that these deficits may contribute to impaired emotion regulation via difficulties disengaging from negatively valenced stimuli (Joormann & Quinn, 2014). In fact, attention biases to negative stimuli have been associated with impaired mood recovery and greater stress vulnerability (Clasen, Wells, Ellis, & Beevers, 2013; Sanchez, Vazquez, Marker, LeMoult, & Joormann, 2013) and thus may serve as an intermediate process connecting impairments in attention with the vulnerability to and maintenance of MD.

More generally, abnormal deployment of attention in the presence of valenced stimuli has been consistently associated with MD. Comparisons of depressed and healthy populations have found that depressed individuals generally exhibit preferential allocation of attention to negative stimuli across a number of paradigms (Clasen et al., 2013; Peckham, McHugh, & Otto, 2010). A meta-analysis of eye-tracking studies found that MD was also associated with less attention to positive stimuli (i.e., an anhedonic bias; Armstrong & Olatunji, 2012). In addition, attention biases also appear to contribute to other information processing biases in depression, such as interpretation and memory biases (e.g., Everaert, Grahek, & Koster, 2016). These negative attention biases are predictive of prospective depression symptom severity, even after accounting for baseline symptom severity, up to 2 years later (Disner, Shumake, & Beevers, 2016; Price et al., 2016). Furthermore, both attention deficits and attentional biases are associated with increased risk for suicidal behavior (e.g., Cha, Najmi, Park, Finn, & Nock, 2010; Keilp et al., 2008). These findings in sum suggest that studying both valenced and nonvalenced aspects of attention in the context of MD may allow us to better understand the pathophysiology of MD and design interventions that more directly target the risk and maintenance factors contributing to a depressive episode.

Of note, there is now preliminary evidence indicating that nonvalenced processes of attention are associated with attentional biases to negative stimuli. Hakamata, Matsui, and Tagaya (2014) found that stronger attention biases to threatening stimuli in healthy individuals was primarily associated with weaker performance on general measures of attention (but not other constructs, like working memory) in a neuropsychological assessment battery. These results suggest that nonvalenced and negatively valenced aspects of attention are related in healthy populations and may extend to depressed populations.

This Study

Despite the abundance of literature regarding attention as an impaired process in neuropsychological studies and as a biased process for valenced information in depressed individuals, only a handful of studies to our knowledge have focused on both valenced and nonvalenced aspects of attention in the context of a single research study in depression.

Utilizing the Stroop task, Hill and Knowles (1991) found that although color-naming took longer on the color incongruent portion of the conventional Stroop and all parts of the emotional Stroop for the entire sample (subclinically depressed and nondepressed students), there were no between-group differences. In addition to using a nonclinical sample and lacking depression severity measures or diagnostic assessments, the researchers provided no a priori hypotheses regarding the conventional Stroop task and did not posit any relationship between the conventional Stroop and emotional Stroop (i.e., between selective attention and valenced information processing). Kerr, Scott, and Phillips (2005) used MD patients as a clinical comparison group to bipolar patients who were either manic, depressed, or euthymic. They found that all patient groups performed worse than controls on all portions of the conventional Stroop task as well as all conditions of the emotional Stroop. Although Kerr and colleagues did propose hypotheses regarding the performance of depressed patients on the conventional and emotional

Stroop tasks separately, they did not hypothesize about or examine their possible interrelation.

Thus, although a relationship between nonvalenced and valenced processes of attention have been suggested based on theory, functional neuroanatomy, and a study with a healthy population, this relationship has not been explicitly explored in depressed individuals. Consequently, we sought to examine different aspects of attention across the clinical spectrum (i.e., never depressed controls, formerly depressed, and currently depressed) to identify potential trait and state effects of major depressive episodes on attentional processes. In addition, we wanted to clarify the specificity of these impairments by comparing with another executive function closely associated with attention, set shifting. Furthermore, we were interested in examining the interrelationship between nonvalenced and valenced processes of attention.

We hypothesized that depression status (i.e., never depressed, formerly depressed, or currently depressed) would be associated with selective attention as well as valenced information processing. We hypothesized that currently depressed individuals would show a greater impairment in selective attention and a stronger bias for negative information than the formerly depressed and never depressed participants. We also hypothesized that the formerly depressed individuals would display poorer performance on measures of selective attention than the never depressed controls. As impairments in other cognitive processes have not been demonstrated as consistently, we did not hypothesize a relationship between depression status and set shifting. Finally, given preliminary research connecting nonvalenced attentional processes with attention biases, we hypothesized that these potential deficits in selective attention would moderate the relationship between depression status and valenced information processing, with currently depressed individuals exhibiting slower selective attention displaying stronger negative attention biases than other groups (e.g., formerly depressed or never depressed individuals with slower selective attention).

Method

Participants

Participants were recruited via community flyers, online postings, and the subject pool of the University of Southern California. Adults between 18 and 45 years of age who were fluent in English were screened by phone, exclusion criteria being a history of major head trauma, brain damage, or neurological disorder. Also excluded were nonnative English speakers. Participants meeting criteria for lifetime history of a major depressive episode (MDE) were recruited for this study, with presence of psychotic symptoms an exclusionary criterion; depression groups were differentiated by whether their MDE was current or lifetime. Individuals who only met for lifetime history of a MDE were considered formerly depressed, whereas those individuals meeting criteria for a MDE at time of assessment were considered currently depressed; no other characteristic was considered in defining the two depressed groups. Never depressed participants were screened for a lifetime history of an MDE and a recent (i.e., 1-year) history of Axis I disorders. A total of 91 people were eligible to participate in and completed the study (26 currently depressed, 30 formerly depressed, and 29 never depressed; 6 individuals had unclear designations despite a clinical interview, e.g., experiencing symptoms for the past 1.5 weeks rather than past 2 weeks, and were consequently excluded); 2 participants were unable to complete the Emotional Stroop Task.

Measures

Baseline clinical assessment. The MINI International Neuropsychiatric Interview (MINI) is a structured clinical interview assessing for Axis I diagnoses of the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*; American Psychiatric Association [APA], 1994). The MINI has been shown to have acceptably high reliability and validity (Sheehan et al., 1998).

Attention tasks

Color-Word interference test (Delis, Kaplan, & Kramer, 2001). The Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference Test is a variation of the standard Stroop paradigm. A total of 50 color words are presented in different colored ink (e.g., the word RED printed in green ink). Subjects were asked to name the color of the ink the word is printed in as quickly as possible without making mistakes. Time to complete the task was recorded for each subject. The Stroop task is a well-established measure of selective attention and response inhibition with demonstrated reliability and validity (Delis et al., 2001; MacLeod, 1991).

Emotional Stroop task. The Emotional Stroop task is a modification of the original Stroop task, substituting valenced words (e.g., fail, sad, good, joy, etc.) for color words. The Emotional Stroop parallels the format of the D-KEFS Color-Word Interference Test. Each set of valenced words was presented separately, in counterbalanced order. The Emotional Stroop task is a widely utilized measure of attentional bias in depression (Epp, Dobson, Dozois, & Frewen, 2012; Peckham et al., 2010).

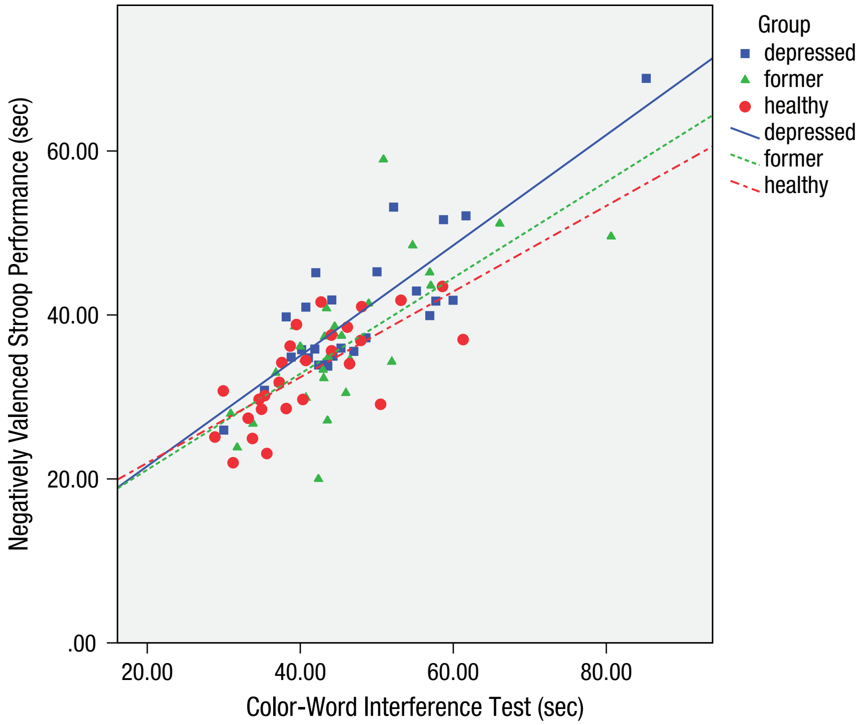

Fig. 1. Association between Color-Word Interference Test and negatively valenced Stroop (and best-fit lines by group).

D-KEFS Trail Making Test (Delis et al., 2001). The D-KEFS version of the Trail Making Test assesses visual scanning and psychomotor speed, along with higher-level functions such as mental flexibility and set shifting. Condition A of the D-KEFS Trail Making Test (Trails A) presented subjects a sheet with numbers and letters printed across the entirety of the page. Subjects were required to draw a line from one number to the next, in numerical order, up to the number 16. Condition B of the D-KEFS Trail Making Test (Trails B) required subjects to switch between connecting numbers and letters in numerical and alphabetical order, respectively (i.e., 1 – A – 2 – B – 3 – C, etc.), up to the letter P. In both conditions, errors were immediately noted by the examiner and subjects were required to correct their mistake before proceeding. A psychomotor speed condition required subjects to trace a multisegment line around the page. Time taken to complete each condition was recorded.

Questionnaires

Depression severity. Current depression severity was evaluated through the Beck Depression Inventory–II (BDI-II; Beck, Steer, & Brown, 1996). It has high test-retest reliability, validity with both normal and clinical samples, and high internal consistency (Dozois, Dobson, & Ahnberg, 1998). In this study, internal consistency was excellent (α = .94).

Beck Anxiety Inventory (BAI). Current anxiety was assessed through the BAI. The BAI has demonstrated adequate test-retest reliability and validity (Beck, Epstein, Brown, & Steer, 1988). In this study, internal consistency was excellent (α = .93).

General knowledge task. The Vocabulary subtest of the Wechsler Adult Intelligence Scale–IV (WAIS-IV; Wechsler, Coalson, & Raiford, 2008) was used to assess general knowledge. This 30-item subtest is administered by a trained interviewer and requires participants to define words, one at a time, in increasing order of difficulty. The test stops after the subject is unable to correctly define three consecutive words.

Procedure

All potential participants were initially screened by phone by trained research assistants. Subjects were then scheduled to come in by the following week to complete the research protocol and study visit. After reviewing and obtaining informed consent, trained graduate students in a PhD program in clinical psychology administered the MINI. Any participants not meeting study criteria at that time were excluded. The participants were then administered the Color-Word Interference Test and Emotional Stroop Task. Participants then completed questionnaires

Table 1. Group Characteristics (e.g., Demographics, Clinical Characteristics, Performance on Each Outcome)

Characteristic	Currently depressed (n = 26)	Formerly depressed[a] (n = 30)	Never-depressed controls (n = 29)
Age	23.12 (6.19)	23.87 (6.32)	24.10 (6.77)
Sex (male, female)	6, 20	10, 20	11, 18
Vocabulary score	41.46 (7.28)	43.10 (7.65)	43.03 (8.27)
Beck Depression Inventory–II	23.19 (10.16)***	7.60 (7.16)	5.86 (7.90)
Beck Anxiety Inventory	16.23 (11.18)***	7.73 (8.28)	5.41 (8.79)
Depression characteristics			
Age of onset	17.46 (3.99)	17.59 (4.61)	—
Range	8–27	11–35	—
Number of episodes	3.77 (4.12)	4.27 (6.18)	—
Stroop Task–C/W Interference	47.87 (11.11)*	45.92 (10.08)†	41.39 (8.06)
Trails A–Number Sequencing	24.61 (6.99)	25.34 (10.20)	24.10 (9.48)
Trails B–Letter Number Sequencing	61.43 (24.43)	61.80 (28.06)	57.19 (21.65)
Emotional Stroop Task–Positive Words	40.99 (8.52)**	35.42 (8.26)	34.11 (7.05)
Emotional Stroop Task–Negative Words	40.33 (8.74)***	36.29 (8.54)†	31.97 (7.97)

Note: Values are means with standard deviations in parentheses, unless otherwise noted.
[a]Mean time recovered for the formerly depressed group was 2.21 years (SD = 2.38).
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$ when compared to the never-depressed group (not controlling for potential covariates such as age).

before they were administered the Vocabulary subtest of the WAIS-IV and the D-KEFS Trail Making Test. Finally, participants were debriefed and compensated $30 or course credit for their participation. The research study was approved by the appropriate institutional review boards and human subjects organizations.

Data analysis

Hierarchical linear regression was used to predict performance on the tasks described earlier. Age and gender were entered in the first step of these linear regressions. Psychomotor speed and current anxiety were entered as a second step to control for neuropsychologically or clinically relevant covariates. Subsequently, group status was entered into the regression model as a main effect to examine unique contributions of group status to the explained variance of the model. For the valenced information processing outcomes, selective attention (i.e., performance on the D-KEFS Color-Word Interference Test) was then entered as the fourth step in our regression models. We then entered a group status × selective attention moderator term for the Emotional Stroop task outcomes to test whether the relationship between group status and attention bias was moderated by selective attention ability.

Listed p-values are all two-tailed. Alpha was set at the .05 level, but given the exploratory nature of this research we also report marginal values (i.e., $.05 < p < .10$) to reduce Type II error.

Results

Descriptives

Table 1 shows group characteristics, means, and standard deviations of demographic and clinical characteristics, as well as performance on each outcome. There was no significant difference in age, $F(2, 82) = 0.17$, $p = .841$, or general knowledge, $F(2, 82) = 0.39$, $p = .68$, nor any differences in gender ratio, $\chi^2(2) = 0.056$, $p = .973$, across the three groups. Age was correlated with performance on the Stroop, Trails A/B, and Emotional Stroop (all $p < .05$), supporting the inclusion of age as a covariate for this study's analyses.

Regression of group status onto neuropsychological functioning

Color-Word Interference Test performance. Table 2 shows results for the hierarchical linear regression analyses for the neuropsychological measures (i.e., the Color-Word Interference Test and Trail Making Test). Demographics were associated with a significant increase in explained variance when added to the model predicting nonvalenced/classic Stroop performance, $F(3, 83) = 4.48$, $p = .006$, with age positively associated with time taken to complete the test. The addition of current anxiety and psychomotor speed also accounted for a significant portion of explained variance, $F(2, 81) = 5.72$, $p = .005$. Psychomotor speed, but not anxiety, was positively associated with Stroop performance, as well as age.

Table 2. Hierarchical Linear Regression for Neuropsychological Measures

Outcome	Parameter estimate (*SE*)	R^2	ΔR^2	*p* value
Stroop C/W Interference		9.85%	9.85%	.002
[Demographics]**				
Age**	0.46 (0.16)			.005
Sex	–0.14 (2.20)			.835
Stroop C/W Interference [Demo +		22.36%	12.51%	.005
Psychomotor Speed + Anx]**				
Age**	0.47 (0.16)			.004
Sex	–1.00 (2.23)			.655
Psychomotor Speed**	0.62 (0.18)			.001
Anxiety	0.13 (0.10)			.198
Stroop C/W Interference [Demo +		28.02%	5.66%	.032
Speed + Anx + Group]*				.003
Age**	0.48 (0.15)			.577
Sex	–1.22 (2.18)			.002
Psychomotor Speed**	0.61 (0.19)			.849
Anxiety	0.02 (0.11)			.052
Group†	[Categorical]			
Trails A–Number Sequencing		32.71%	8.64%	.007
[Demographics]**				
Age***	0.66 (0.13)			<.001
Sex	–0.46 (1.82)			.799
Trails A–Number Sequencing [Demo +		33.31%	9.24%	.021
Psychomotor Speed + Anx]*				
Age***	0.67 (0.13)			<.001
Sex	–0.76 (1.85)			.684
Psychomotor Speed**	0.49 (0.15)			.002
Anxiety	0.07 (0.08)			.400
Trails A–Number Sequencing [Demo +		33.36%	0.05%	.840
Speed + Anx + Group]				<.001
Age***	0.67 (0.13)			.677
Sex	–0.78 (1.88)			.003
Psychomotor Speed**	0.50 (0.16)			.502
Anxiety	0.06 (0.09)			.970
Group	[Categorical]			
Trails B–Letter Number Sequencing		23.16%	12.04%	.001
[Demographics]**				.007
Age**	1.06 (0.39)			.109
Sex	–8.65 (5.33)			
Trails B–Letter Number Sequencing		23.16%	12.04%	.006
[Demo + Psychomotor Speed + Anx]**				
Age**	1.06 (0.39)			.008
Sex	–8.64 (5.46)			.118
Psychomotor Speed***	1.59 (0.45)			<.001
Anxiety	–0.00 (0.24)			.993
Trails B–Letter Number Sequencing		24.44%	1.28%	.683
[Demo + Speed + Anx + Group]				
Age**	1.07 (0.39)			.008
Sex	–9.00 (5.50)			.106
Psychomotor Speed***	1.64 (0.47)			<.001
Anxiety	–0.13 (0.27)			.622
Group	[Categorical]			.518

†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Including group status in the regression model significantly improved R^2, $F(1, 80) = 4.74$, $p = .032$. In this fourth model, age and psychomotor speed were significant predictors of selective attention, whereas group was moderately associated with selective attention ($p = .052$). Least squares means comparisons (i.e., controlling for demographics, psychomotor speed, and anxiety) showed that currently depressed individuals were significantly slower than the never depressed group ($p = .015$) but not significantly different from the formerly depressed group ($p = .151$), and with no significant difference between the formerly depressed and never depressed groups ($p = .242$). These results suggest that currently depressed individuals have impaired selective attention relative to never depressed controls, even after controlling for age, psychomotor speed, and anxiety. After controlling for anxiety, psychomotor speed and demographics, formerly depressed individuals appear to show an intermediate level of impairment on the Color-Word Interference Test, falling in between currently and never depressed individuals (though these differences between formerly depressed individuals and the other two groups were not statistically significant).

Trail Making Test. On the Trail Making Test, demographics were associated with performance on Trails A, $F(3, 83) = 13.00$, $p < .001$, and Trails B, $F(3, 83) = 5.13$, $p = .003$. Inclusion of psychomotor speed and current anxiety also significantly increased R^2 in the regression models for Trails A, $F(2, 81) = 4.07$, $p = .021$, and Trails B, $F(2, 81) = 5.48$, $p = .006$. The addition of clinical group also was not associated with a significant change in explained variance for either Trails A, $F(1, 80) = 0.04$, $p = .840$, or Trails B, $F(1, 80) = 1.03$, $p = .682$. This finding suggests that depression status was not associated with visual scanning, mental flexibility, or set shifting as measured by these tasks.

Regression of group status onto attentional bias

Negative-valenced Stroop task. Table 3 shows results for the hierarchical linear regression analyses for the Emotional Stroop task. Demographics were marginally associated with negatively valenced Stroop task performance, $F(3, 81) = 2.29$, $p = .085$. Inclusion of psychomotor speed and current anxiety was associated with a moderate increase in R^2, $F(2, 79) = 2.39$, $p = .098$, with age remaining a significant predictor and current anxiety showing a moderate association with negatively valenced Stroop performance. The addition of group status did significantly increase explained variance, $F(1, 77) = 9.47$, $p = .003$, with group status and age as significant predictors of task performance in the regression model. Examination of least squares means comparisons found that the depressed group was marginally slower than the formerly depressed ($p = .058$) and significantly slower than never depressed groups ($p = .002$) in negatively valenced Stroop performance, and that formerly depressed individuals were not significantly slower than never depressed controls ($p = .124$). Including the main effect of selective attention led to a significant increase in R^2, $F(1, 77) = 44.05$, $p < .001$, with selective attention as the sole significant predictor of negative attentional bias. The addition of a moderation term was not associated with a significant increase in explained variance, $F(1, 76) = 0.40$, $p = .529$. To clarify the relationship between depression status, selective attention, and negative attentional bias we explored additional analyses.

Post hoc analyses. Although the relation between group status and attention bias did not vary as a function of selective attention (i.e., a clear moderation effect; see Fig. 1 for a graphical representation of this general relationship between selective attention and negative attentional bias), reduction of the main effect of group on attentional bias after inclusion of the main effect of selective attention may suggest that the relationship between group status and attention bias is explained by selective attention performance (i.e., mediation or an indirect effect; cf. Baron & Kenny, 1986). We tested this post hoc question by utilizing an ordinary least squares path analysis-based approach to examine direct and indirect effects of proposed mediators in our models (implemented through PROCESS, a computational and analytic modeling tool in SAS; Hayes, 2012; SAS version 9.2, SAS Institute, Cary, NC). This approach explicitly quantifies the indirect effect of a mediator on an outcome and tests whether or not this effect is significant through asymmetric bootstrap confidence intervals (see Hayes, 2009, for further discussion of the use of bootstrapping over other methods for statistical significance testing for mediators). This study employed a 95% bias-corrected bootstrap confidence interval in our mediation analyses to test whether indirect effects had a significant effect on the outcome. An indirect effect is considered significantly different from zero if its 95% bootstrap confidence interval is entirely above or below zero. For the negatively valenced Stroop, the indirect effect of selective attention was statistically different from zero for the currently depressed group (95% bootstrap CI: 0.93 to 8.44) but not for the formerly depressed (95% bootstrap CI: -0.95 to 4.81) or never depressed group (95% bootstrap CI: -4.76 to 1.01).[1]

Positively valenced Stroop task. Neither demographics, psychomotor speed, nor anxiety was associated with performance on the positively valenced Stroop task. The addition of group status led to a significant increase in explained variance, $F(1, 78) = 9.49$, $p = .003$, with least squares means comparisons again showing that currently depressed individuals performed significantly slower

Table 3. Hierarchical Linear Regression for Attention Bias Measures

Outcome	Parameter estimate (*SE*)	R^2	ΔR^2	*p* value
Negatively Valenced Stroop [Demo + Speed + Anx]†		11.19%	5.78%	.098
Age*	0.32 (0.15)			.040
Sex	–1.14 (2.16)			.600
Processing Speed	0.24 (0.18)			.185
Anxiety†	0.17 (0.09)			.071
Negatively Valenced Stroop [Demo + Speed + Anx + Group]**		22.13%	10.95%	.003
Age*	0.32 (0.15)			.033
Sex	–1.43 (2.05)			.487
Processing Speed	0.23 (0.17)			.179
Anxiety	0.04 (0.10)			.651
Group**	[Categorical]			.006
Negatively Valenced Stroop [Covariates + Group + Selective Attention]***		58.83%	36.69%	<.001
Age	0.02 (0.11)			.880
Sex	–0.70 (1.51)			.644
Processing Speed	–0.15 (0.13)			.271
Anxiety	0.03 (0.07)			.652
Group	[Categorical]			.112
Selective Attention (Stroop Interference Trial)***	0.64 (0.08)			<.001
Negatively Valenced Stroop [Covariates + Group + Attn. + Moderator]		59.36%	0.53%	.529
Age	0.02 (0.12)			.888
Sex	–0.70 (1.57)			.660
Processing Speed	–0.16 (0.14)			.243
Anxiety	0.04 (0.07)			.623
Group	[Categorical]			.901
Selective Attention (Stroop Interference Trial)***	0.54 (0.18)			<.001
Moderation Term (Group × Selective Attn)	[Categorical]			.623
Positively Valenced Stroop [Demo + Speed + Anx]		7.15%	3.92%	.210
Age	0.23 (0.15)			.123
Sex	–0.00 (2.07)			.999
Processing Speed	0.20 (0.17)			.242
Anxiety	0.13 (0.09)			.167
Positively Valenced Stroop [Demo + Speed + Anx + Group]**		18.13%	10.97%	.002
Age	0.23 (0.14)			.106
Sex	–0.38 (1.97)			.849
Processing Speed	0.25 (0.17)			.135
Anxiety	0.00 (0.09)			.992
Group**	[Categorical]			.008
Positively Valenced Stroop [Covariates + Group + Selective Attention]***		61.83%	43.70%	<.001
Age	–0.08 (0.10)			.444
Sex	0.38 (1.36)			.783
Processing Speed	–0.14 (0.12)			.247
Anxiety	–0.01 (0.06)			.861
Group†	[Categorical]			.052
Selective Attention (Stroop Interference Trial)***	0.38 (1.36)			<.001
Positively Valenced Stroop [Covariates + Group + Attn. + Moderator]		62.20%	0.37%	.600
Age	–0.09 (0.10)			.415
Sex	0.19 (1.42)			.891
Processing Speed	–0.14 (0.12)			.264
Anxiety	–0.01 (0.07)			.904
Group	[Categorical]			.972
Selective Attention (Stroop Interference Trial)***	0.62 (0.13)			<.001
Moderation Term (Group × Selective Attn)	[Categorical]			.702

Note: ΔR^2 for [Demo + Processing Speed + Anxiety] model is compared to the R^2 for the [Demographics only] model (not shown).
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

than formerly depressed (p = .007) or never depressed individuals (p = .005) and no difference between formerly and never depressed individuals (p = .817). Inclusion of selective attention was associated with a significant improvement in R^2, $F(1, 77) = 59.00$, $p < .001$, with selective attention significantly predicting performance on the positively valenced Stroop and group moderately predicting performance. Examination of least squares means comparisons found that currently depressed individuals performed significantly slower than formerly depressed individuals (p = .016) but not never depressed individuals (p = .117), with no significant difference between formerly and never depressed individuals (p = .394). Given the pattern of results, we again investigated whether or not there was an indirect effect of selective attention on the relation between group and positive attentional bias. For the positively valenced Stroop, the indirect effect of selective attention was statistically different from zero for the currently depressed group (95% bootstrap CI [0.78, 8.66]) but not for the formerly depressed (95% bootstrap CI [–0.98, 4.88]) or never depressed group (95% bootstrap CI [–4.88, 0.92]).

Taken together, these findings suggest that the attentional bias found in depressed individuals is associated both with clinical status and with selective attention abilities. Although currently depressed individuals as a whole exhibited slower performance on the negatively valenced Stroop task relative to formerly depressed and never depressed individuals, this group effect is mediated by selective attention (particularly in currently depressed individuals). With regard to attentional biases toward positive stimuli, clinical status and selective attention were both associated with bias as well, with currently depressed individuals showing slower performance on the positively valenced Stroop task relative to formerly and never depressed individuals. Similar to the negatively valenced attentional bias, selective attention has an indirect effect on the relationship between clinical group and performance on the positively valenced Stroop, particularly for currently depressed individuals.

Discussion

Depressed individuals show impairment in selective attention, even after remission of the depressive episode, as well as attention biases for negative information (Peckham et al., 2010; Rock et al., 2014). Both forms of cognitive dysfunction have received increasing attention in this field, whether as a cognitive vulnerability or as a point of intervention (Joormann & Gotlib, 2010; Murrough, Iacoviello, Neumeister, Charney, & Iosifescu, 2011). Although previous researchers (i.e., Hill & Knowles, 1991; Kerr et al., 2005) have examined both constructs in the context of the same study, they did not follow up with further analyses testing for associations between selective attention and attention biases, nor included a formerly depressed sample in addition to their control group to aid in discerning between state versus trait effects of depression. Both studies were also relatively underpowered, as Hill and Knowles (1991) had a *total* of 24 participants, whereas the largest group size in Kerr et al.'s (2005) study was 18 participants.

The results of the present study did not support the hypothesis that deficits in selective attention moderate the relationship between depression status and valenced information processing. Rather, post hoc analyses suggested that deficits in selective attention mediate the relationship between depression status and valenced information processing, even after adjusting for covariates such as age, psychomotor speed, and anxiety. Decreased performance on measures of selective attention was associated with stronger biases in valenced information processing. This relation was apparent only in currently depressed individuals, as formerly and never depressed individuals did not show the same indirect effect. Our findings provide support for the close relationship among valenced and nonvalenced facets of attention in depressed individuals.

Unexpectedly, this relationship encompassed both negatively and positively valenced attentional biases as assessed by the Emotional Stroop Task. Although this observed relationship between valenced and nonvalenced aspects of attention may be related to the similarity of the Color-Word Interference Test and valenced versions of the Stroop, the indirect effect found only extended to our currently depressed group and not the formerly or never depressed groups. Our results may suggest that the emotional biases assessed by the Stroop task may not be clearly distinct. Indeed, previous studies examining negatively and positively valenced biases in the Emotional Stroop Task have found no differences between biases in clinically depressed groups (e.g., Kerr et al., 2005). However, it is worth noting that the attentional biases characterized by the Emotional Stroop Task exhibit concurrent and predictive validity, having been associated with depression severity and suicidal behavior (Cha et al., 2010; Epp et al., 2012). Undoubtedly, additional follow-up is needed to explore this relationship between valenced and nonvalenced aspects of attention with other tasks. Regardless, as difficulties disengaging from negative stimuli have been associated with reduced recovery from stress (Sanchez et al., 2013), the results of the present study suggest impaired attentional disengagement as a possible target of intervention for currently depressed individuals.

Impairments in selective attention have been consistently found in currently depressed and formerly depressed individuals, as well as in individuals at risk for depression, suggesting that selective attention deficits are a trait-like marker for depression. In contrast, there is less support for attentional biases for valenced information among individuals who are currently remitted from depression (e.g., Merens, Booij, & Van Der Does, 2008), implying that attentional biases may be a more state-like marker of depression. These previous findings, in conjunction with our current results, would suggest that additional factors play a role in the appearance of attention biases for depressed individuals. Thus, although greater impairments in selective attention are associated with stronger attention biases for valenced information in currently depressed individuals, the presence or absence of attention biases may be dependent on other state-like factors.

Depression status and neuropsychological performance

Our other study hypotheses were partially supported. Depression status was associated with deficits in selective attention (i.e., impaired performance on the Color-Word Interference Test; but not set shifting). This finding adds to the large body of literature that shows the Stroop task to be consistently sensitive to the impact of depression (e.g., Ardal & Hammar, 2011). Although performance on the Stroop has, at times, been suggested to be related to psychomotor retardation (i.e., Lemelin & Baruch, 1998), we found no impairment in performance on another timed/speed-based measure of attention, the Trail Making Test. We also controlled for psychomotor speed in our analyses. Consequently, our results show that this impairment in attention is specific to selective attention and not tied to a general psychomotor retardation. Controlling for psychomotor speed may also explain why our formerly depressed group did not show significant impairments relative to the never depressed group; previous studies that have examined these two groups often did not control for such factors.[2]

Depression status was also associated with valenced information processing on the Emotional Stroop task. Consistent with previous studies, the Emotional Stroop task demonstrated significant differences in performance between clinical and nonclinical groups (Epp et al., 2012). The Emotional Stroop task might be a measure sensitive to the impact of depression on valenced information processing due to the amount of cognitive resources required to complete the task. The impact of task demands on sensitivity to the effects of depression on task performance is reflected in contrasting performance on the classic Stroop task versus the Digit Span Forward test, as Digit Span Forward performance is often not significantly impacted by many disorders of the brain (much less depression; Lezak et al., 2004), whereas the Stroop task appears sensitive to the effects of depression even in some instances when individuals are currently euthymic (e.g., Xu et al., 2012).

Limitations

Our study had a number of limitations that merit discussion. Despite the fact that our subjects met criteria for an MDE, our sample was mild to moderate in depression severity range, which may limit the ability to generalize our findings to more severe depressive episodes (e.g., those requiring inpatient treatment). For example, individuals exhibiting depression with psychotic features show a different neuropsychological profile from individuals who are depressed without psychotic features (Fleming, Blasey, & Schatzberg, 2004), suggesting that our results might not necessarily generalize to that clinical population. That being said, the severity levels present in this study are more common in the general clinical population (i.e., mild to moderately depressed individuals).

We did not control for current antidepressant medication usage. However, antidepressant usage has not been demonstrated to significantly impact neuropsychological functioning (Porter, Robinson, Malhi, & Gallagher, 2015). Antidepressant use has been shown to have an impact on mood-congruent attentional biases though (Browning, Holmes, & Harmer, 2010), leaving open the possibility that our results may be partially muddled by use of antidepressant medication. Unfortunately, we did not collect detailed information on medication usage and could not control for it in our analyses. However, a significant proportion of studies on attentional biases do not evaluate and control for antidepressant usage, suggesting a need for more systematic attention to this issue.

Perhaps our most significant limitation was the lack of multiple measures of selective attention and attentional bias. This limitation is not specific to our study, however, as a number of studies often assess these constructs only with a single measure (e.g., the dot-probe task). Unfortunately, within this field a number of tasks have been sorted under these broad umbrella constructs and the heterogeneity in findings may be due in part to the utilization of different tasks and measures to assess these constructs. This issue may particularly be compounded by differences between tasks that tap processes in relative isolation (e.g., response inhibition in the go/no-go task) compared to tasks that tap these processes under more cognitively demanding conditions (e.g., requiring these processes to be at least partially integrated with other basic cognitive processes, such as selective attention and response inhibition in the Stroop task). Clearly future studies, including our own, ought to employ multiple tasks to broadly capture attention and attentional bias.

Strengths and future directions

Our study recruited a sample of individuals who met *DSM-IV-TR* (APA, 2000) diagnostic criteria for an MDE, whether currently or during the course of their lifetime. A number of studies in this field have employed subclinical or dysphoric individuals (e.g., Farrin, Hull, Unwin, Wykes, & David, 2003), who appear to display relatively less attention bias than individuals meeting diagnostic criteria for MD (though this discrepancy may only be moderate in nature; Peckham et al., 2010). Consequently, studies utilizing those populations may not be accurately characterizing the impact of MD on neuropsychological functioning and basic cognitive processes. In the other causal direction, risk factors such as impairments in attention may not be present in these dysphoric, subclinical populations. Related to this, there is a clear need to study the interrelationship between attention (and other executive functions) and depression in a more longitudinal fashion to understand how they contribute to one another (and more intermediate phenotypes, e.g., rumination, cognitive biases) across the lifespan.

Our samples were recruited from a number of sources (i.e., community bulletin boards, flyers, psychology subject pool), improving the generalizability of our results. Of note, each group came from multiple recruitment sources, reflecting a lack of systematic group differences aside from depression status (supported in part by the lack of differences in age or general knowledge across the three groups). In addition, our subjects were recruited from a community sample rather than treatment centers, suggesting that their clinical history is more reflective of the general population than for individuals actively seeking or involved in treatment.

Although deficits in attention may exist prior to depression onset and appear associated with familial risk for depression more than clinical history (Hsu et al., 2014), attention does appear amenable to change as interventions have been able to significantly improve selective and executive attention (Chiesa, Calati, & Serretti, 2011). This set of findings would suggest that a reduction in biases for negative information for currently depressed individuals could be achieved by training in/strengthening of basic cognitive processes (i.e., selective attention). Preliminary evidence is emerging to support such nonvalenced attentional control/cognitive control interventions as a method of reducing symptoms of depression or associated, underlying processes (e.g., rumination; Hoorelbeke et al., 2015; Siegle et al., 2014).

In summary, the present study is the first to test the relation between selective attention and attention biases for valenced information across depression status. Results suggest an indirect effect of impairments in selective attention on the relationship between current depression diagnosis and biases in valenced information processing. The findings identify a possible mechanism underlying a maintaining factor for currently depressed individuals (i.e., attention bias) and support development of further nonvalenced attentional control or cognitive control interventions for depression.

Author Contributions

K. J. Hsu developed the study concept. All authors contributed to the study design. Testing, data collection, data analyses, and interpretation were performed by K. J. Hsu. The initial draft of the manuscript was written by K. J. Hsu, with G. C. Davison providing valuable commentary and revisions. All authors approved the final version of the manuscript for submission.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Notes

1. As our independent variable (i.e., depression status) is multicategorical, we dummy coded group status and estimated effects by treating one group variable as the independent variable and another as a covariate, swapping the process a total of three times to account for the three categories in our independent variable. This recommended approach allowed us to estimate individual group effects and differences in mediation (Hayes, 2012).
2. Moreover, when running a basic analysis of variance between the three groups on the nonvalenced Stroop (not shown in results), the pattern of performance previously demonstrated in the literature (i.e., no significant differences between currently

and formerly depressed individuals, with both groups performing worse than never depressed controls) was found in our sample.

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